“EFFECT OF ANTIEPILEPTIC DRUGS ON SERUM LIPID PROFILE IN CHILDREN WITH EPILEPSY IN A TERTIARY CARE HOSPITAL – A CASE CONTROL STUDY”

Dissertation submitted in partial fulfilment of university regulations

For the award of degree of

M.D. PAEDIATRICS

BRANCH VII

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CERTIFICATE

This is to certify that the dissertation entitled **"EFFECT OF ANTIEPILEPTIC DRUGS ON SERUM LIPID PROFILE IN CHILDREN WITH EPILEPSY IN A TERTIARY CARE HOSPITAL – A CASE CONTROL STUDY"** submitted by **DR.PON DIVYA** 2015-2018 session at Madras Medical College to the faculty of Paediatrics, The Tamilnadu Dr. M.G.R Medical University, Chennai in partial fulfilment of the university rules and regulations for award of **M.D., Degree in Paediatrics** (BRANCH VII) is a bonafide research work carried out by him under our direct supervision and guidance.

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DECLARATION

This dissertation entitled **"EFFECT OF ANTIEPILEPTIC DRUGS ON SERUM LIPID PROFILE IN CHILDREN WITH EPILEPSY IN A TERTIARY CARE HOSPITAL – A CASE CONTROL STUDY"** is a bonafide work done by **Dr.PON DIVYA** at Institute of Child Health, Madras Medical College, Chennai during the academic year 2015-2018 under the guidance of **Prof. DR.S.LAKSHMI, MD.,DCH,** Professor of Paediatrics, Institute of Child Health and hospital for children, madras medical college, Chennai- 600003. This dissertation submitted to The Tamilnadu Dr.M.G.R. Medical University, Chennai towards partial fulfilment of the rules and regulations for the award of **M.D Degree in Paediatrics** (Branch VII).

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DECLARATION

I, **Dr.PON DIVYA**, solemnly declare that this dissertation entitled **"EFFECT OF ANTIEPILEPTIC DRUGS ON SERUM LIPID PROFILE IN CHILDREN WITH EPILEPSY IN A TERTIARY CARE HOSPITAL – A CASE CONTROL STUDY"** was done by me under the guidance and supervision of **Prof. DR.S.LAKSHMI, MD., DCH.** This dissertation is submitted to The Tamilnadu Dr.M.G.R Medical University, Chennai in partial fulfilment of the rules and regulations for the award of **M.D Degree in Paediatrics (Branch VII).**

Place: Chennai **Dr.PON DIVYA**

Date:

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Last but not the least I would like to thank my husband and family for their constant encouragement and help given to complete my dissertation.

CERTIFICATE –II

This is to certify that this dissertation work titled **"EFFECT OF ANTIEPILEPTIC DRUGS ON SERUM LIPID PROFILE IN CHILDREN WITH EPILEPSY IN A TERTIARY CARE HOSPITAL – A CASE CONTROL STUDY"** of the candidate **DR.PON DIVYA** with registration Number **201517001** for the award of **M.D PAEDIATRICS** in the branch of **VII**. I personally verified the urkund .com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and the result shows **1 percentage** of plagiarism in the dissertation.

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CONTENTS

INTRODUCTION

Hyperlipidemia in young children is an important risk factor for the development of coronary heart disease in later life. Evidence shows that besides high total cholesterol (TC) and triglyceride (TG) concentrations, increased LDL-Cholesterol and decreased HDL-Cholesterol also contribute to cardiovascular diseases. Hence, assessing changes in serum lipid levels following antiepileptic drugs may be helpful in choosing the safest drug and prevention of cardiovascular complications in later life[1]

Multiple risk factors e.g. seizures plus coronary artery disease, could increase the chance of sudden death in patients with epilepsy. Even a subtle myocardial lesion associated with, e.g., end vessel coronary artery disease might expose the patients with epilepsy to sudden unexpected death. Therefore, even small changes in the serum lipid profile could have serious consequences in patients with epilepsy[3].

Many studies have shown significant relationship between serum lipid levels and antiepileptic drugs, especially with the enzyme inducers like Phenytoin, Phenobarbitone and Carbamazepine.

However such studies are lacking in south Indian population. If it is proved that there is a significant association between serum lipid levels and antiepileptic drug usage, they can be cautiously used in those with preexisting risk factors for metabolic syndrome such as family history of atherosclerosis, obesity, dyslipidemia, hypertension, or insulin resistance, so that complications can be prevented at the earlier stage itself. Periodic screening and counseling for lifestyle modifications (low animal dietary fat intake with no calorie restriction) may also be warranted in those situations.[12]

Epilepsy contributes to a prevalence of 5.59 per 1,000 populations. Males and females both are equally affected and are the same in different geographical areas.

According to WHO, epilepsy is one of the most common serious brain disorder that affects not only the individual but also disturbs the family and also the society in general. WHO estimates that 8 per 1000 population worldwide are having epilepsy, with higher prevalence in the developing countries when compared to developed countries. There are approximately 10 million people estimated to be with epilepsy in India accounting for $1/5^{th}$ of the global burden.[1]

Seizure is a transient occurrence of signs and / or symptoms resulting from abnormal excessive or synchronous neuronal activity in the brain.

It is a sudden paroxysmal electrical discharge from the CNS resulting in involuntary motor, sensory or autonomic disturbances with or without alteration in the sensorium.[27]

Epilepsy is a disorder of the brain characterised by an enduring predisposition to generate seizures & by the neurological cognitive, psychological & social consequences.

Epileptic syndrome is a disorder that manifests one or more specific types and a specific age of onset and a specific prognosis.

The type of seizure will depend on the following:

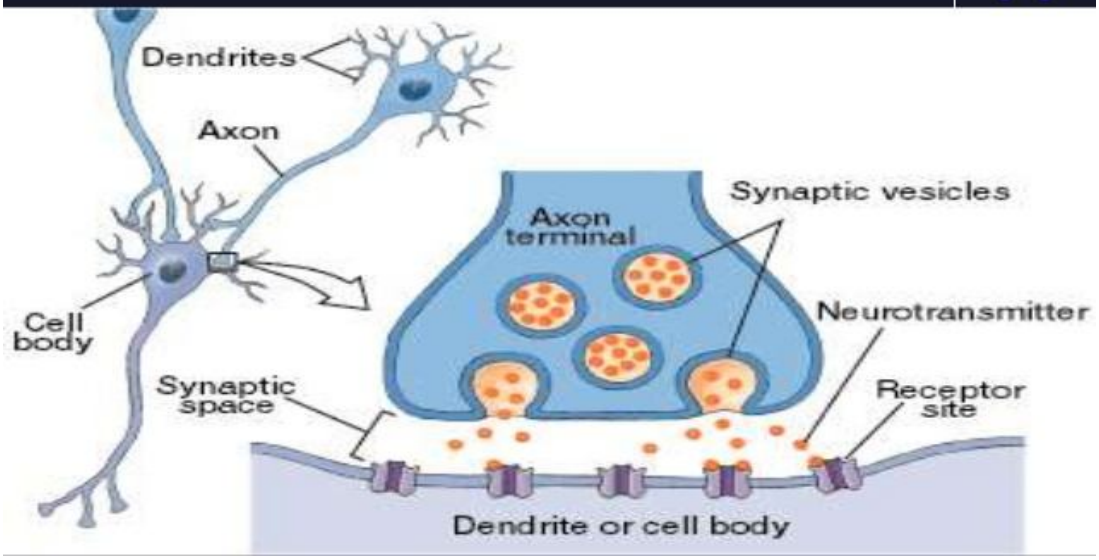
- The area of the brain producing the discharge
- The type of discharge
- The age of the patient

Epileptogenesis occurs due to sequence of events that converts normal neuronal networks into hyperexcitable epileptogenic networks.

Seizures occur because of the abnormality in the neurotransmitters levels / Ion channels or Receptors. These abnormalities can result in hyperexcitability of the neurons, leading to a tendency to seizures.

Other causes that can result in neuronal damage include various insults like infections, trauma and vascular events.

Basic mechanisms of epileptogenesis



Excitatory & inhibitory neurotransmitters

- Glutamate & aspartate – Excitatory neurotransmitters

↓

Induces Ca + ion current

↓

Depolarisation

↓

seizure

Causes of seizures	**Causes of epilepsy**
Infections Viral encephalitis Pyogenic meningitis Tubercular meningitis Neurocysticercosis Metabolic events Hypoglycemia Hypocalcemia Hypomagnesemia Dyselectrolytemia (hypernatremia/hyponatremia) Vascular events Cerebrovascular accidents Drug intoxication/side effects Vascular events Thrombosis Embolism Hemorrhage Neoplasms Hypoxia/anoxia especially during delivery Head trauma Febrile seizures	Cerebral malformations Metabolic diseases Degenerative brain diseases Neoplasms Genetic disorders

Classification of seizures:

1. Generalized is defined as when the epileptic discharge involves both the cerebral hemispheres at the same time

a) Generalized tonic-clonic seizures:

Initiation with a tonic phase characterized by a generalized stiffening of the whole body, followed by rhythmic to and fro contractions of the extremities.

In the tonic phase there may be a tongue bite, with urinary or stool incontinence, and frothing during the clonic phase.

b) Tonic seizures

Sudden but sustained contraction of various muscle groups or the whole body. If the patient is standing, drop attack may result.

c) Atonic seizures

There is a sudden loss of muscle tone of head and neck, trunk or limbs. Drop attack may result and are associated with underlying neurological abnormalities.

d) Clonic seizures:

Rhythmic jerking contractions with relaxation of various muscle groups

e) Myoclonic seizures:

Sudden contraction of a muscle or muscle group,can be single, or occur in clusters or simply myoclonic, or myoclonic tonic/atonic.

f) Absence seizures:

Brief period of alteration of consciousness:

i) Typical absence: Starts and ends abruptly. After the brief period of alteration of consciousness, the child resumes activity as if nothing has happened.

ii) Atypical absence: with a gradual onset, the patient has alteration of consciousness for a variable duration (may be minutes) and ends gradually. Postural changes can occur. Often is associated with other seizure types, neurological abnormalities and mental retardation.

iii) Absence with special features: Eyelid myoclonus, myoclonic absence

2) Focal or partial:

The epileptic discharge starts in a focus of the brain in one hemisphere.

- Without impairment of consciousness/responsiveness:
    - Simple partial seizures
- With impairment of consciousness/responsiveness:
    - Complex partial seizures
    - Secondarily generalized seizures

3) Focal, generalized or unclear:

Epileptic spasms

<u>Antiepileptic drugs:</u>

The antiepileptic drugs are a diverse group of pharmaceuticals that are used in the treatment of epileptic seizures. The goal of an anticonvulsant is to suppress the rapid and excessive firing of neurons that start a seizure. Treatment of epilepsy is often a lifelong affair.[16]

Drugs	Indications	Preparation	Dosage	Side effects
PHENYTOIN	Focal seizures GTCS	Suspension 30 mg/5 mL Tablets 100 mg	5–8 mg/kg/day In two divided doses	Gum hypertrophy, Rash Steven-Johnson syndrome, Toxicity, Ataxia, Nystagmus, Blurring of vision
PHENOBARBITONE	Neonatal seizures Status epilepticus Tonic-clonic Focal seizures Clonic febrile seizures	Tablets 30 mg Syrup 20 mg/5 mL	3–5 mg/kg/day Single dose or two divided doses	Sedation Hyperkinetic behaviour Dependence
SODIUM VALPROATE	Broad spectrum, effective against any seizure type Idiopathic generalized epilepsies— Childhood absence epilepsy, juvenile myoclonic epilepsy, infantile spasms, Lennox-Gastaut syndrome	Tablets 200, 400 mg Syrup 200 mg/5 mL	20–40 mg/kg/day Two divided doses	Hepatotoxicity Drowsiness Lethargy Weight gain, Hyperammonemia Teratogenicity
CARBAMAZEPINE	Focal seizures Generalized tonic clonic seizures	Suspension: 100 mg/5 mL Tablets 200, 400, 600 mg	10–30 mg/kg/day Three divided doses	Rash, Bone marrow depression, Steven Johnson syndrome

CLOBAZAM	Add on drug for any seizure type Intermittent use in Febrile seizures, or seizures due to known recipitating causes	Tabs 5 mg, 10 mg, 20 mg	0.5 mg/kg/day one-two divided doses	Drowsiness Hypotonia

Newer AEDS	**Indications**	**Preparation**	**Dosage**	**Side effects**
Levetiracetam	Add on for myoclonic seizures Focal seizures Primary generalized seizures	Tab 250 mg, 500 mg,	Start with 10 mg/kg/day 20 mg/kg/day increase weekly Increase to 60 mg/kg/day In two divided doses	Headache Anorexia Drowsiness Behaviour problems
Topiramate	Add on Focal/generalized epilepsy West syndrome, Broad spectrum add on drug for epilepsy with multiple types of seizures, e.g. Lennox-Gestaut syndrome	Tab 25 mg, 50 mg, 100 mg, 200 mg	Start with 0.5 mg/kg/day Increase to 5 mg/kg/day Max dose: 8 mg/kg/day	Drowsiness Ataxia, Metabolic acidosis

Older-generation AEDs which are commonly used for the treatment of epilepsy including Phenytoin, Carbamazepine, Phenobarbitone and valproate exert prominent effects on the hepatic enzyme system and may alter metabolic pathways that are related to increased vascular risks.

Microsomal enzyme induction by these drugs can alter the metabolism of bile acids, bilirubin, and other endogenous molecules. One of the important effects of the induced hepatic microsomal enzyme system is on the lipid metabolism.

Antiepileptic drugs alter the metabolism of lipids and drugs due to their enzyme inducing action in the liver function and increase in the activity of hepatic microsomal enzyme system.

The relationship between insulin resistance and fasting lipids is understood through its effect on lipoprotein metabolism. Insulin plays major role in determining triglyceride clearance from the blood via activation of lipoprotein lipase and output of triglycerides through the effects on the synthesis and secretion of VLDL by the liver. Furthermore, insulin controls the free fatty acids output from adipose tissue. In the

insulin-resistant state, triglyceride-rich lipoproteins accumulate in the circulation due to decreased activity of lipoprotein lipase and also increased lipolysis in adipose tissue, and increased movement of VLDL particles out of the liver. This delay in the plasma lipoprotein triglyceride clearance allows for cholesterol esters to be passed on from HDL to triglyceride-rich particles, which results in potential atherogenic lipoprotein particles.

Common antiepileptic drug like phenytoin is metabolised in the liver by hydroxylation and glucuronide conjugation. The kinetics of its metabolism is capacity limited, it changes from first order to zero order over therapeutic range, thus small increments in dose, produce disproportionately high concentrations in the plasma.[21]

Phenytoin is shown to have association with high blood sugar levels. Phenytoin impairs the secretion of insulin and decreases the response of plasma glucose to insulin.

Sodium valproate is completely metabolized in the liver by oxidation and glucuronide conjugation. It causes a decrease in serum free carnitine levels by inhibition of plasmalemmal carnitine uptake having concerns particularly in children younger than 2 years for developing an

idiosyncratic potentially fatal hepatotoxic syndrome. Hyperinsulinism and insulin resistance can also occur with sodium valproate.[21]

With the concerns of hepatotoxicity and derangement of lipid profiles necessitating monitoring, this study was planned to evaluate and compare the effects of commonly used antiepileptic drugs on serum lipid levels in children.

Carbamazepine does not influence endogenous cholesterol synthesis or intestinal absorption directly. The increase is rather due to changes in the conversion cascade of IDL particles.

Carbamazepine stimulates the hepatic synthesis of cholesterase and increase the formation and pool size of bile acids, which in turn raise the level of intestinal absorption of cholesterol by facilitating micelle formation.

Prolonged treatment with phenytoin is often accompanied by various metabolic and endocrine abnormalities. In the pancreatic βcells, it inhibits the release of insulin and suppresses the response of plasma insulin to various stimuli, thus increasing the levels of serum lipids. It also acts by inducing the CYP enzyme (CYP51) enzyme which is a housekeeping

gene of the cytochrome P450 super family, which is involved in cholesterol biosynthesis in humans. The CYP450 enzyme system is involved in the synthesis and metabolism of cholesterol.[21]

Many studies have proved that Levetiracetam is not found to affect the hepatic microsomal system, whereas sodium valproate causes inhibition of the hepatic enzyme system.

REVIEW OF LITERATURE

1. In a study conducted by Manimegalai et al, they observed statistically significant high mean TC, HDL-C, LDL-C and TG levels in the phenytoin group and also statistically significant high mean TC, HDL-C and TG levels in the group receiving oxcarbazepine. However, no significant difference was observed in the mean LDL-C levels when compared to control. There was no statistical significance among mean TC, HDL-C, LDL-C and TG levels in the group receiving valproate and Levetiracetam.

2. Study conducted by Rakesh et al showed significantly higher level of total cholesterol in children taking phenytoin and carbamazepine. Children taking valproate had no significant difference in the values of total cholesterol. Levels of triglycerides and HDL-C did not show any significant differences.

3. In a study conducted by Aditi dhir et al, Children who took valproate had significantly higher mean serum triglyceride and total cholesterol when compared to children on phenytoin monotherapy

4. In a study done by Kantoush et al, children who received sodium valproate for 6 months had lower serum levels of TC, triglycerides, LDL-C, VLDL-C and higher HDL-C levels than controls. Also CBZ, PB and PHT, which are enzyme-inducing drugs, caused significant increase of serum levels of TC, LDL-C and HDL-C. CBZ also had caused significant increase of triglycerides and VLDL-C.

5. Scott Mintzer et al conducted a study in the epilepsy patients who were made to switch from phenytoin and carbamazepine to non inducer drugs, produced significant declines in total cholesterol and triglycerides. Patients who stopped taking carbamazepine also had a significant decline in lipoprotein levels.

6. Muzamil M Mugloo et al had reported in his study that statistically significant high mean TC was found in the group receiving phenytoin for 6 months or beyond when compared with valproic acid or control group. However, there was no statistically significant difference among mean TC, HDL-C, LDL-C, TG levels in the group receiving valproic acid when compared with control group.

7. Pooja dewan et al had concluded in her study that the mean total cholesterol in children on phenytoin therapy was significantly higher than the control group. Serum triglycerides, low density lipoprotein cholesterol, very low density lipoprotein cholesterol, and HDL-C cholesterol, were not significantly different from control group.

8. Yilmaz et al, concluded in his study that the Serum TC, HDL-C, LDL-C and TG concentrations increased after 3 months of treatment with carbamazepine. Serum lipid levels showed no significant alterations by treatment with sodium valproate. Serum TG levels increased after 3 months of treatment with phenobarbitone and remained high after 1 year but no difference was found for TC, for HDL-C,and for LDL-C values.

9. Elena Pita Calandre, Blanca Sinuks Porta, and Dolores Garcia de la Calzada, *Epilepsia,* 33(1):154-157, 1992,New York International League Against Epilepsy conducted a study on the effect of chronic phenytoin treatment on serum lipid profile in epileptic patients and found that patients showed higher HDL cholesterol,

apolipoproteins A &A1, GGT levels and lower LDL-C cholesterol and apolipoprotein B values

10. P Kumar, Y Rai et al studied on the effect of anticonvulsant Drugs on Lipid Profile in Epileptic Patients, The Internet Journal of Neurology. 2003 Volume 3 Number 1, found a significant increase in serum levels of triglyceride, total cholesterol, HDL-C and VLDL-C in patients receiving combination therapy of either Phenytoin and Phenobarbitone or Phenytoin and Carbamazepine or Phenytoin alone. Patients receiving Carbamazepine alone had significant increase in serum levels of triglyceride and VLDL-C but no significant changes in serum levels of total cholesterol & HDL-C in this group. A significant correlation between duration of anticonvulsant therapy and lipid profile was established in this study.

11. Fatma Mujgan Sonmez, Ercan Demir, Asim et al, *J Child Neurol* 2006, in their study on effect of Antiepileptic Drugs on Plasma Lipids, Lipoprotein and Liver Enzymes, total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, apolipoprotein A and apolipoprotein B

levels, and liver enzymes were determined before the initiation of the treatment and at 3, 6, and 12 months of the treatment period. The mean pre-treatment lipid levels among the groups were not significantly increased. The mean lipoprotein (a) levels were significantly increased in all groups at 3, 6, and 12 months of the treatment period.

12. Yaser et al, conducted a study on the relationship of serum lipids and thyroid hormone level changes in epileptic children on valproate mono therapy, where he concluded that Valproate has no effect on either lipids or thyroid functions in epileptic children treated with that drug

13. J.M. Eiris et al, conducted a study on effects of long-term treatment with antiepileptic-drugs on serum lipid levels in children with epilepsy. In the groups receiving carbamazepine or phenobarbitone, mean TC, HDL-C, and LDL-C levels were higher than in the control group. In the group receiving valproate, mean TC level, mean LDL-C level, mean HDL-C was significantly lower than in the control group. In none of the treated groups mean VLDL-C or TG level differ significantly from the corresponding control-group

14. Hasan Tekgul et al, concluded in his study on Serum Lipid Profile in Children Receiving Anti-epileptic drug monotherapy that when the Serum levels of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TGs), apolipoprotein Al and apolipoprotein B were measured at baseline and after 2 years of AED monotherapy,it did not cause a significant level of concern for an atherogenic effect in children with epilepsy**.**

AIM AND OBJECTIVES OF THE STUDY:

AIM OF THE STUDY:

To estimate the serum lipid levels in children with seizure disorder on antiepileptic monotherapy for more than 6 months.

PRIMARY OBJECTIVE:

To assess the effect of commonly used antiepileptic drugs on serum lipid levels in epileptic children

SECONDARY OBJECTIVE:

To compare the effect of newer antiepileptic drugs with conventional drugs on serum lipid levels.

STUDY JUSTIFICATION

Changes in serum lipids caused by long-term anticonvulsive treatment have often been discussed controversially. In the previous studies done on the effect of hepatic enzyme-inducing AEDs on serum lipid profiles, the samples have mostly comprised of adults. Only a few studies have been done on children and also the results are conflicting with regard to the variable trends observed in the lipid parameters.[22] The highest incidence of epilepsy in children coupled with the need of long term antiepileptic treatment could lead to development of metabolic complications at an early age the risk of atherosclerosis has been the main point of discussion. The Expert Panel on Blood Cholesterol Levels on Children and Adolescent of National Educational Cholesterol Program (NCEP, 1992) suggests that prevention of premature atherosclerosis should begin early in the childhood. Children are likely to be more vulnerable to any potential factor unfavourably affecting their metabolic status.[16] Thus assessing changes in serum lipid levels following antiepileptic drugs may be useful to choose the safest drug and prevention of cardiovascular complications in later life.

SUBJECTS AND METHODS:

STUDY DESIGN: Case control study

STUDY PLACE: Department of general paediatrics and Department of pediatric neurology, Institute Of Child Health and Hospital for Children, Egmore.

STUDY PERIOD: February 2017 to September 2017

INCLUSION CRITERIA:

- Children on anticonvulsant monotherapy for at least 6 months and in follow up in the child neurology department of ICH.

EXCLUSION CRITERIA:

- Children with diseases that alter the serum lipid profile for eg. nephrotic syndrome

- Children on drugs that affect the serum lipid profile for eg,corticosteroids
- Children on combination antiepileptic drug therapy.
- Children having thyroid disorder or other endocrinopathies.
- Children with chronic liver, heart or renal disease, progressive neurological or psychiatric illness
- Guardians who refused to give consent were excluded.

SAMPLE SIZE:

With an alpha error of 5% and beta error of 20%, for a 95%confidence interval, sample size required are 33 for phenytoin, 42 for phenobarbitone group, 20 for levetiracetam, 20 for carbamazepine and 40 for sodium valproate group

ETHICS:

Written informed consent was obtained from all parents and institution review board clearance was obtained.

MATERIALS AND METHODS

After obtaining the written and informed consent from the parent/ guardian of the children, a clinical evaluation was performed as per a predesigned proforma.

The information regarding the age, sex, type of seizures, duration of the antiepileptic drug immunotherapy, dose of the antiepileptic drug, any family history of stroke or cardiovascular disease were collected followed by a detailed systemic examination.

Height and weight was calculated as per the standard procedure. Anthropometry measurements were taken for each child. Standing height (cm) was measured with a standard calibrated stadiometer, and the body weight (kg) was noted on a standard weighing scale with children dressed in minimal clothing.

The study population were divided into two groups: cases which include children receiving AEDs for more than 6 months and controls as healthy children.

A blood sample (3 ml) was drawn after an overnight fast for serum glucose, liver enzymes, total cholesterol, HDL-C, LDL-C, TG measurement.

Total cholesterol was assessed by using cholesterol oxidase peroxidase enzyme method. High-density lipoprotein cholesterol was measured by direct enzymatic analysis method and serum triglycerides by glycerol peroxidase method. All these parameters were assessed by the COBAS C 311 analyzer.

Very low density cholesterol and low density lipoprotein cholesterol were calculated using Friedewald formula :

LDL Cholesterol= (Total Cholesterol)- (HDL Cholesterol)- (Triglycerides/5)

VLDL-C = Triglycerides/5

STATISTICAL ANALYSIS

All data were entered in Microsoft excel sheet and was imported to SPSS software. All analysis were performed using SPSS, Version 20.0 Chi square test was performed to find out the significance of correlation between the data and p value of < 0.05 was considered statistically significant. The means of the groups were compared by independent t test.

OBSERVATION AND RESULTS

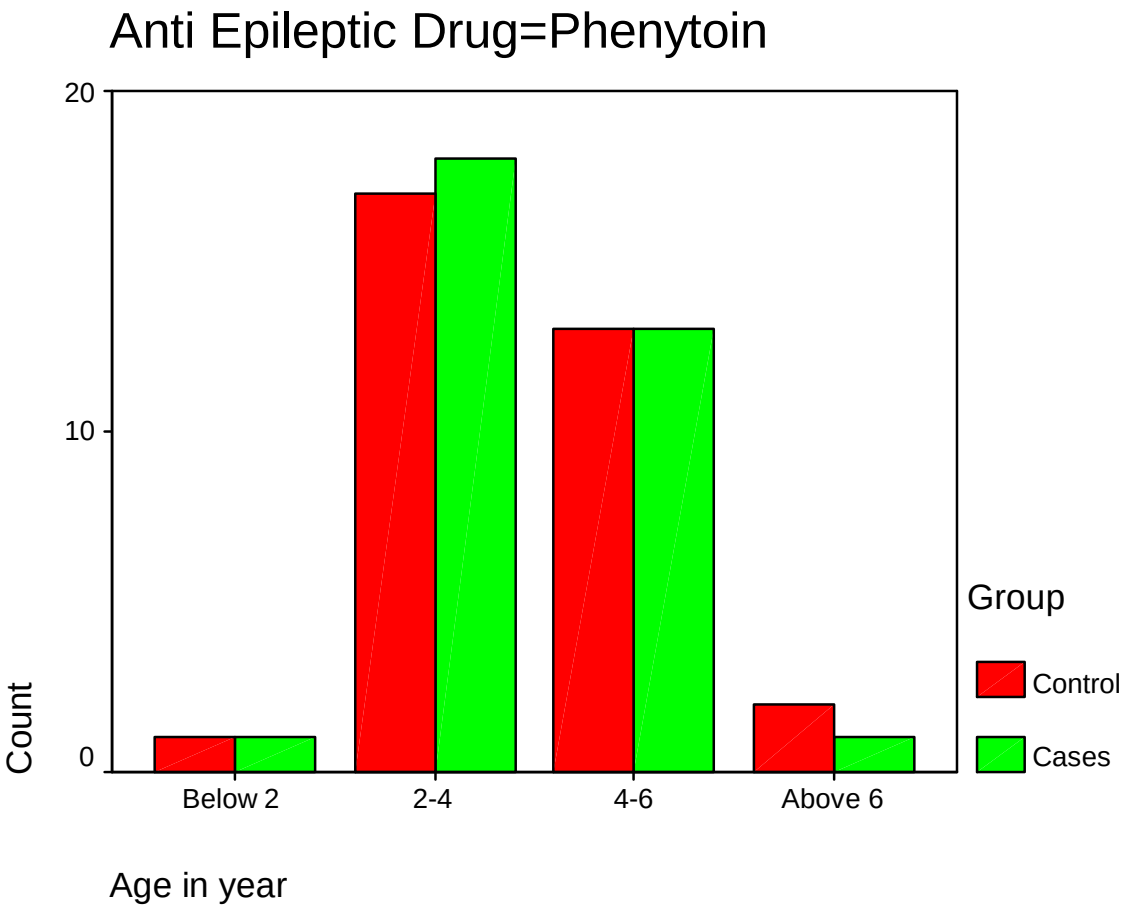
PHENYTOIN

Age in years- Anti Epileptic Drug- PHENYTOIN

AGE	GROUP		TOTAL	P Value
	CASES	CONTROL		
<2YR	1	1	2	.948
2-4YR	17	18	35	
4-6YR	13	13	26	
>6YR	2	1	3	
TOTAL	33	33	66	

Above table shows the various age groups in the phenytoin group consisting of 2 children in age group <2yrs, 35 children in the age group between 2-4yrs,26 in 4-6yrs and 3 above 6yrs coming to a total of 66,out of which 33 are cases and 33.

Majority of the children in the phenytoin group were in the 2-4yrs age group range.

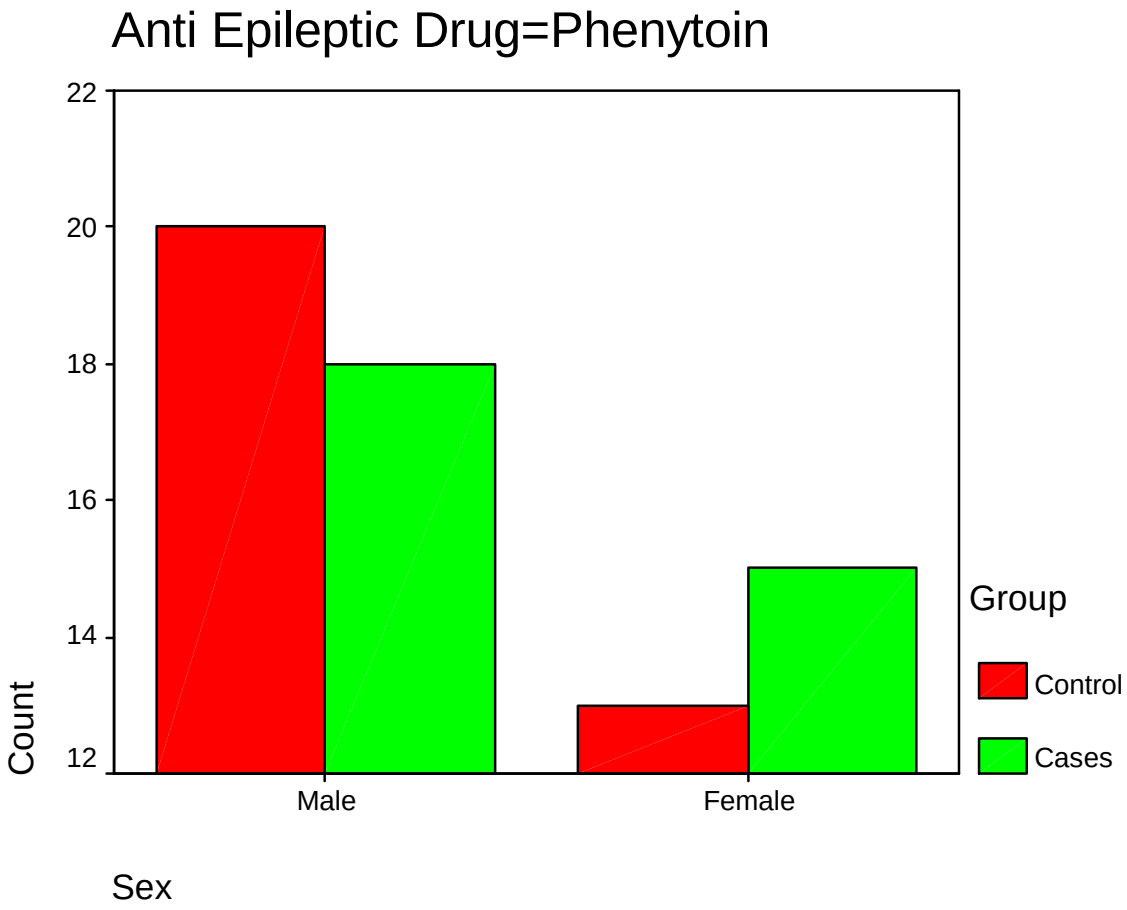


Sex * Group * Anti Epileptic Drug – PHENYTOIN

SEX	GROUP		TOTAL	P Value
	CASES	CONTROL		
MALE	20	18	38	0.618
FEMALE	13	15	28	
TOTAL	33	33	66	

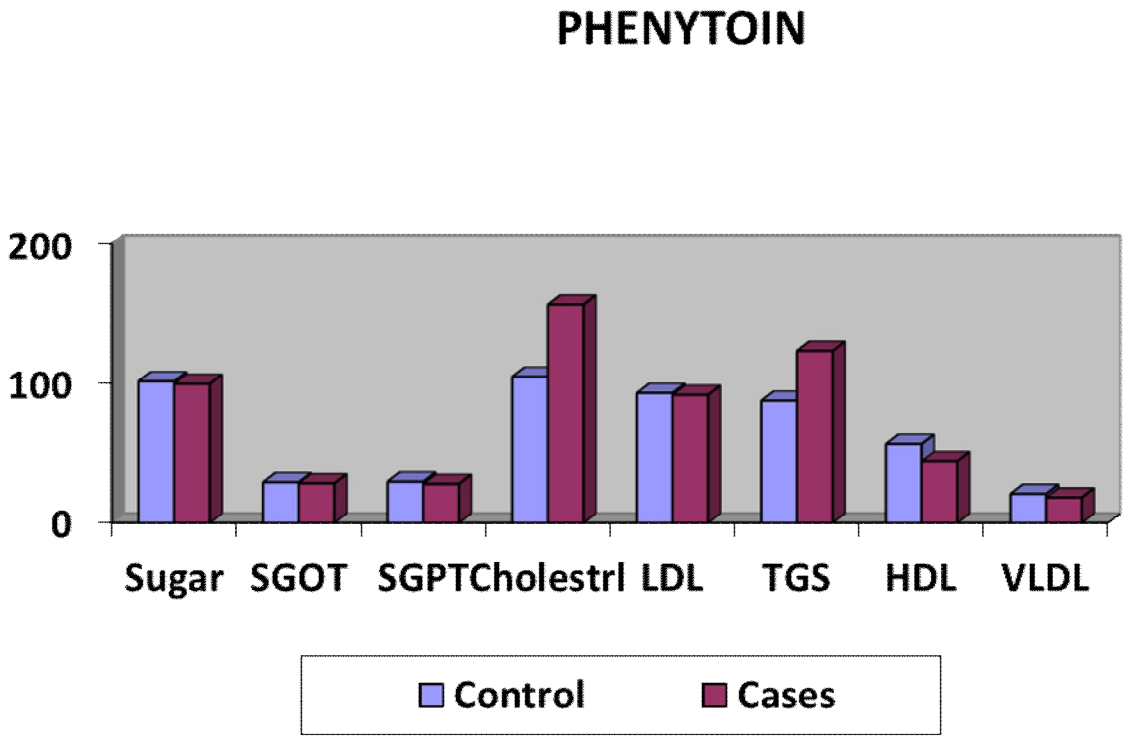
Sex distribution was shown in the above table.

Out of 66 children, 38 consist of males and 28 were females. Control group had 20 male and 13 females, case group had 18 male and 15 females.



Comparison of variables in the phenytoin group

	PHENYTOIN GROUP				P value
	Control		Cases		
	Mean	SD	Mean	SD	
Sugar	101.73	22.26	99.97	24.46	0.761
SGOT	29.12	7.35	28.33	5.07	0.614
SGPT	29.58	5.15	27.88	5.87	0.216
Cholestrl	105.03	8.60	156.73	31.93	0.000
LDL	93.36	6.81	92.06	24.33	0.768
TGS	87.88	12.16	123.48	25.99	0.000
HDL	56.73	12.56	44.52	10.14	0.000
VLDL	20.82	7.38	18.18	9.00	0.198



Above table shows the comparison between the various components like sugar, sgot, sgpt, Total cholesterol, Triglycerides, HDL-C, LDL-C, VLDL-C with the cases and controls.

The values of the sugar were almost equal and did not have any statistical significance in the cases and control group.

The liver enzymes including SGOT and SGPT also did not get affected in both cases and control group.

Whereas the Total cholesterol and Triglyceride levels were significantly high with the p value of 0.000 when compared to control groups.

HDL-C level was in the lower range in the cases when compared to the control groups.

LDL-C and VLDL-C levels did not show any statistical significance when compared in both the groups.

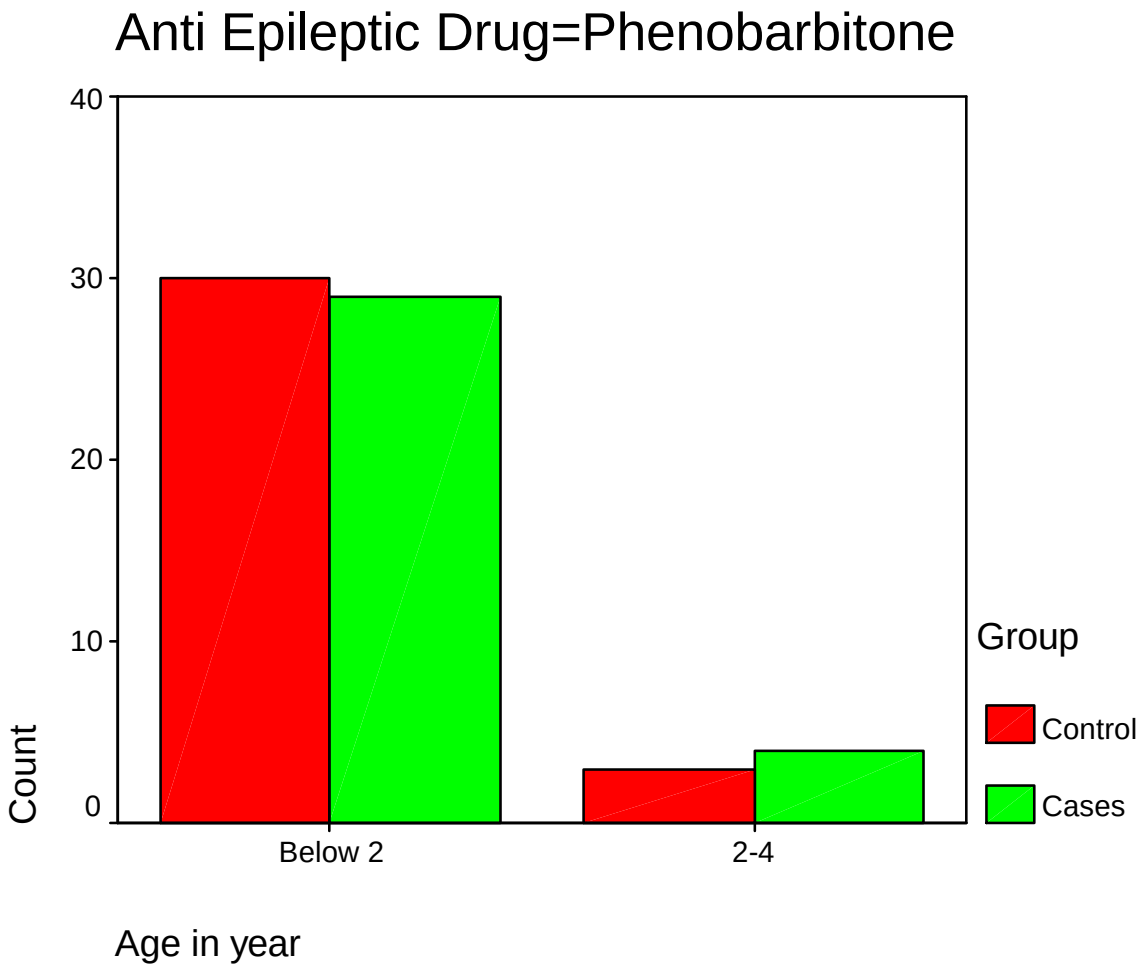
PHENOBARBITONE

B) Age in year * Group * Anti Epileptic Drug

AGE	GROUP		TOTAL	P Value
	CASES	CONTROL		
<2YR	30	29	59	.689
2-4YR	3	4	7	
TOTAL	33	33	66	

As depicted in the above table, in contrary to the previous group, this phenobarbitone group has almost 59 cases in the age group of less than 2 yrs. In the 2-4 yrs age group there were 7 children. Above 4 yrs, no children took phenobarbitone tablets in the study.

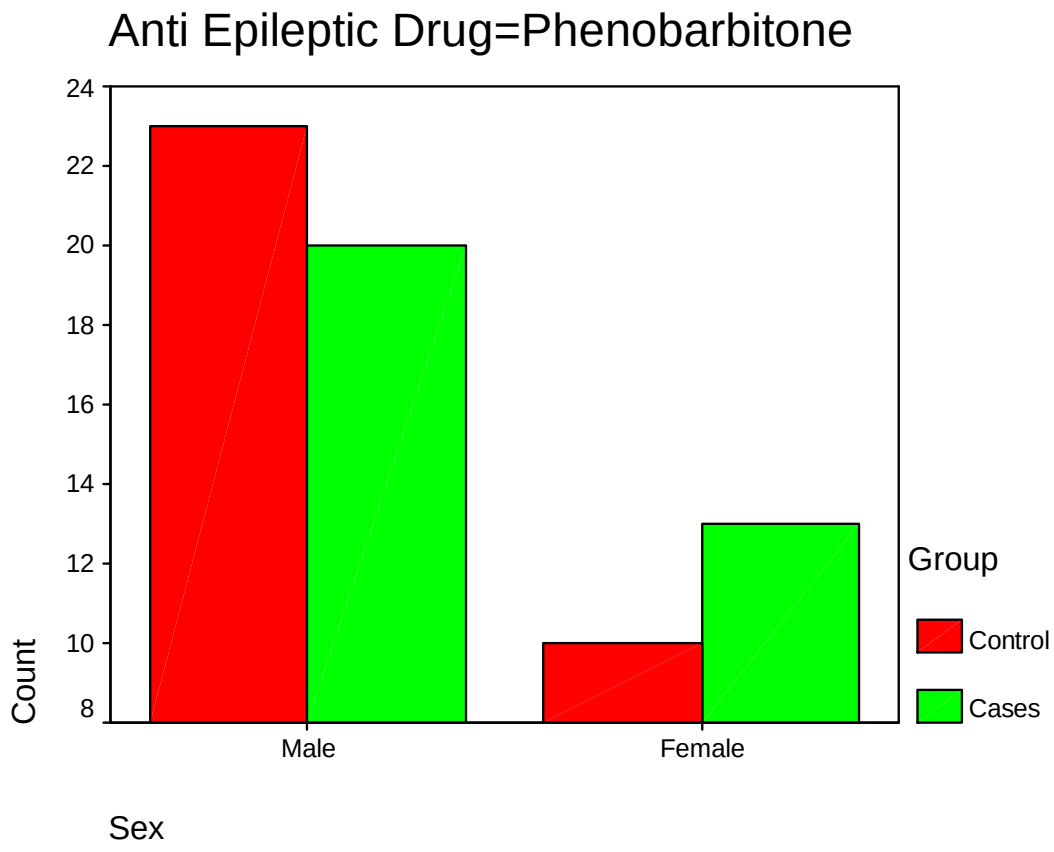
Phenobarbitone is most commonly used in less than 2 yrs old children.


Anti Epileptic Drug=Phenobarbitone
40
30
20
10
0
Count
Below 2
2-4
Age in year
Group
Control
Cases

Sex * Group * Anti Epileptic Drug – PHENOBARBITONE

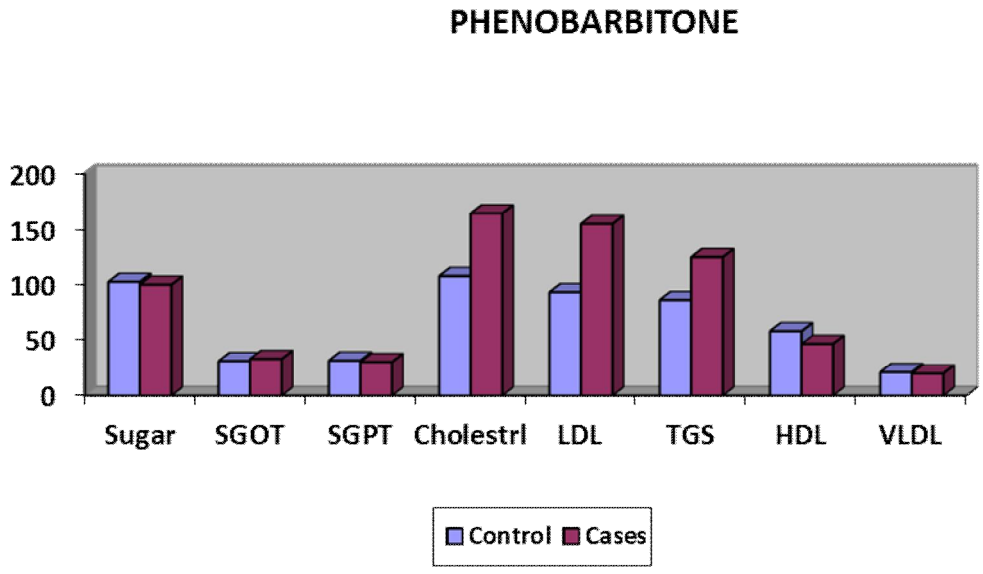
SEX	GROUP		TOTAL	P Value
	CASES	CONTROL		
MALE	23	20	43	0.438
FEMALE	10	13	23	
TOTAL	33	33	66	

In this group, 43 were boys and 23 were girls coming to a total of 66.



Comparison of variables in the phenobarbitone group

	PHENOBARBITONE GROUP				P Value
	Control		Cases		
	Mean	SD	Mean	SD	
Sugar	102.61	19.01	99.97	24.46	0.627
SGOT	30.88	7.81	32.73	6.31	0.294
SGPT	31.21	7.63	29.97	5.63	0.454
Cholesterol	107.76	9.28	164.97	34.41	0.000
LDL	93.36	6.81	155.27	28.55	0.000
TGS	86.30	8.12	125.55	42.19	0.000
HDL	57.73	14.41	46.30	9.47	0.000
VLDL	20.82	7.38	19.64	8.70	0.554



As like the previous group, there were no significant difference between sugar levels, SGOT and SGPT levels in the cases and control group. Whereas the total cholesterol, triglyceride and LDL-C were all increased in the children who were taking phenobarbitone drug with the mean values of 164.97, 125.55, and 155.27 when compared with the control group. HDL-C was decreased in the case group when compared with that of the control group. VLDL-C was not altered in both the groups of children.

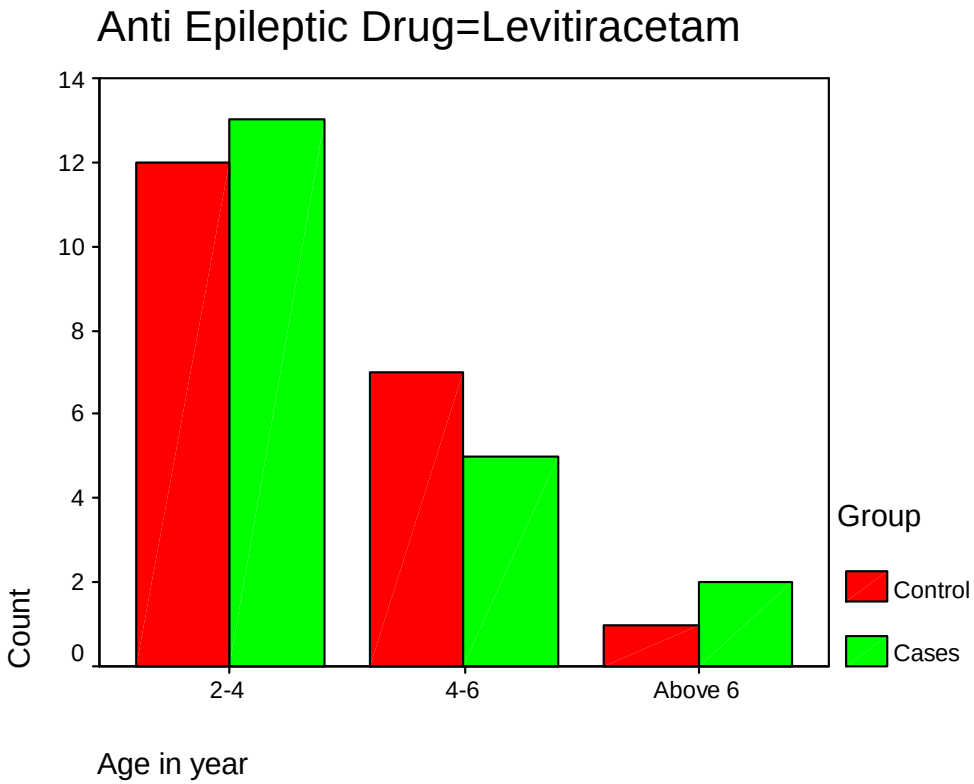
LEVETIRACETAM

Age in year * Group * Anti Epileptic Drug

AGE	GROUP		TOTAL	P Value
	CASES	CONTROL		
2-4YR	12	13	25	0.702
4-6YR	7	5	12	
>6YR	1	2	3	
TOTAL	20	20	40	

Above table shows that there are 25 children in the age group of 2-4 yrs, 12 in the age group 4-6 yrs, and 3 children in the age group above 6yrs, totally coming to 40 in number including both cases and controls.

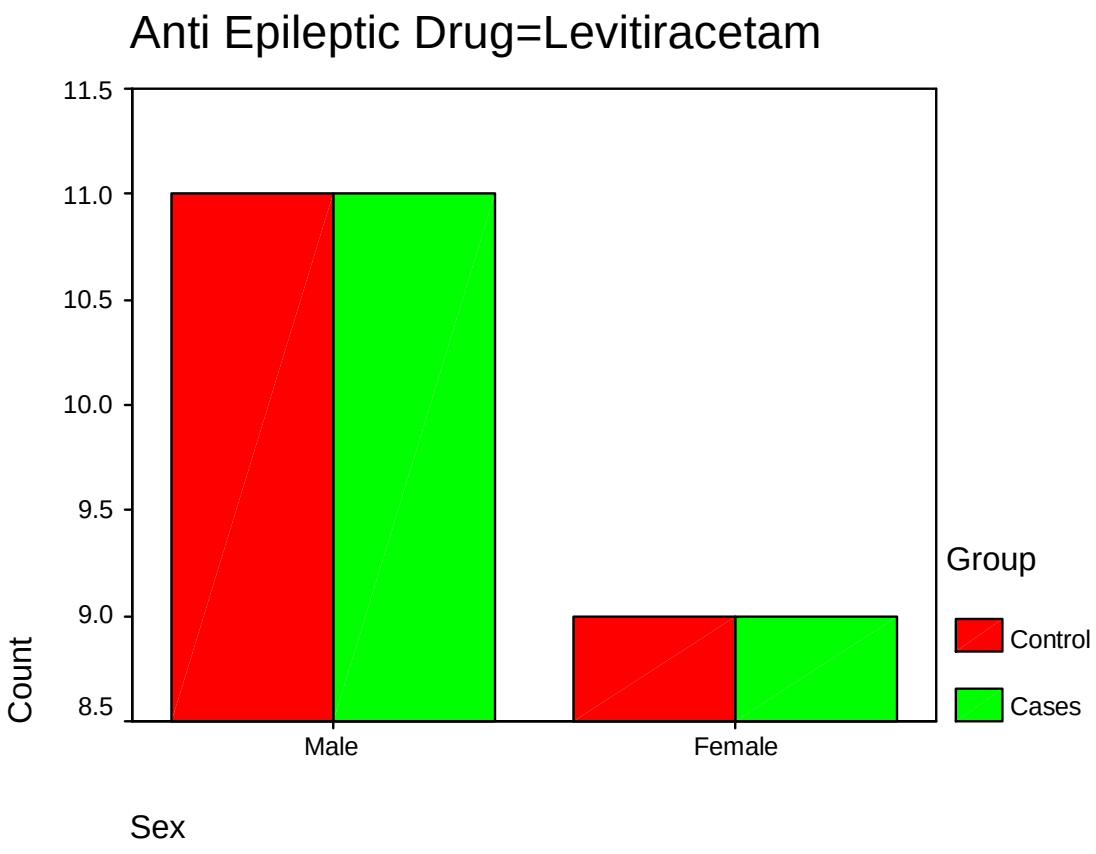
This shows that no children below the age of 2 yrs were taking Levetiracetam drug in this study.


Anti Epileptic Drug=Levitiracetam
14
12
10
8
6
4
2
0
Count
2-4
4-6
Above 6
Age in year
Group
Control
Cases

Sex * Group * Anti Epileptic Drug

SEX	GROUP		TOTAL	P Value
	CASES	CONTROL		
MALE	11	11	22	1.000
FEMALE	9	9	18	
TOTAL	20	20	40	

There was 22 boys and 18 girls who participated in this group, coming to a total of 40. There was no significance between the two groups.



Comparison of variables in the Levetiracetam group:

	Group				P Value
	Control		Cases		
	Mean	SD	Mean	SD	
Sugar	99.40	20.99	109.00	25.15	.198
SGOT	32.40	8.41	38.15	12.99	.105
SGPT	32.55	9.83	38.05	9.51	.080
Cholesterol	112.15	13.55	118.85	10.67	.091
LDL	82.45	12.12	84.90	11.67	.519
TGS	85.40	6.29	83.65	6.20	.381
HDL	53.30	9.68	49.30	5.27	.113
VLDL	28.45	4.45	27.65	6.61	.656

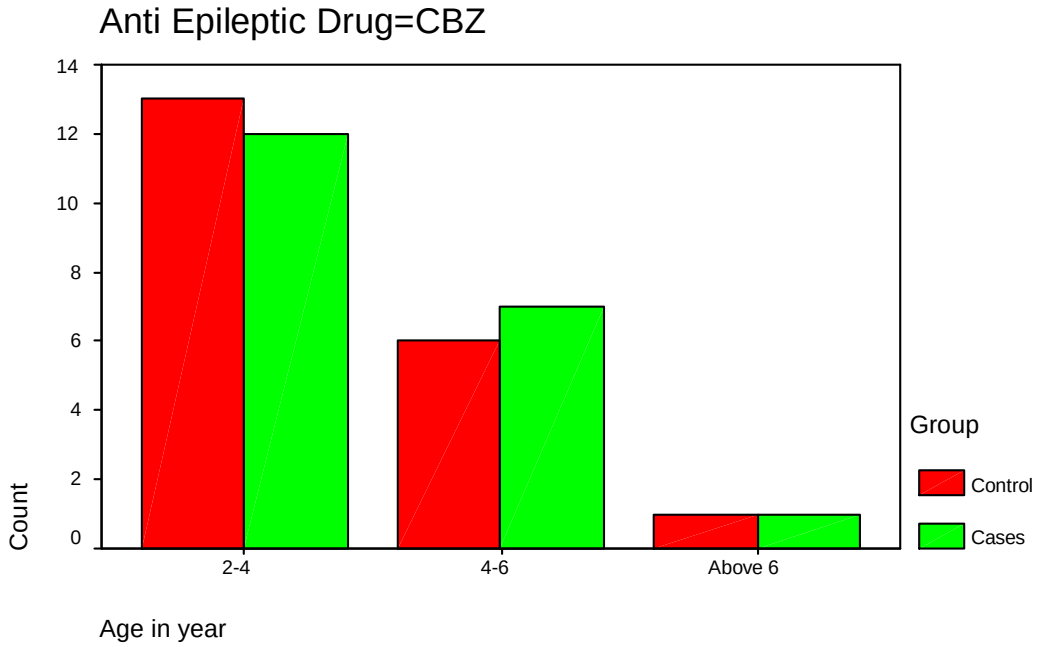
In the cases and control group of Levetiracetam, there were no statistical significance in the values of sugar, SGOT, SGPT, total cholesterol, HDL-C, LDL-C, VLDL-C and triglycerides when compared with the control and cases group.

CARBAMAZEPINE:

Age in year * Group * Anti Epileptic Drug – CARBAMAZEPINE

AGE	GROUP		TOTAL	P Value
	CASES	CONTROL		
2-4YR	13	12	25	0.943
4-6YR	6	7	13	
>6YR	1	1	2	
TOTAL	20	20	40	

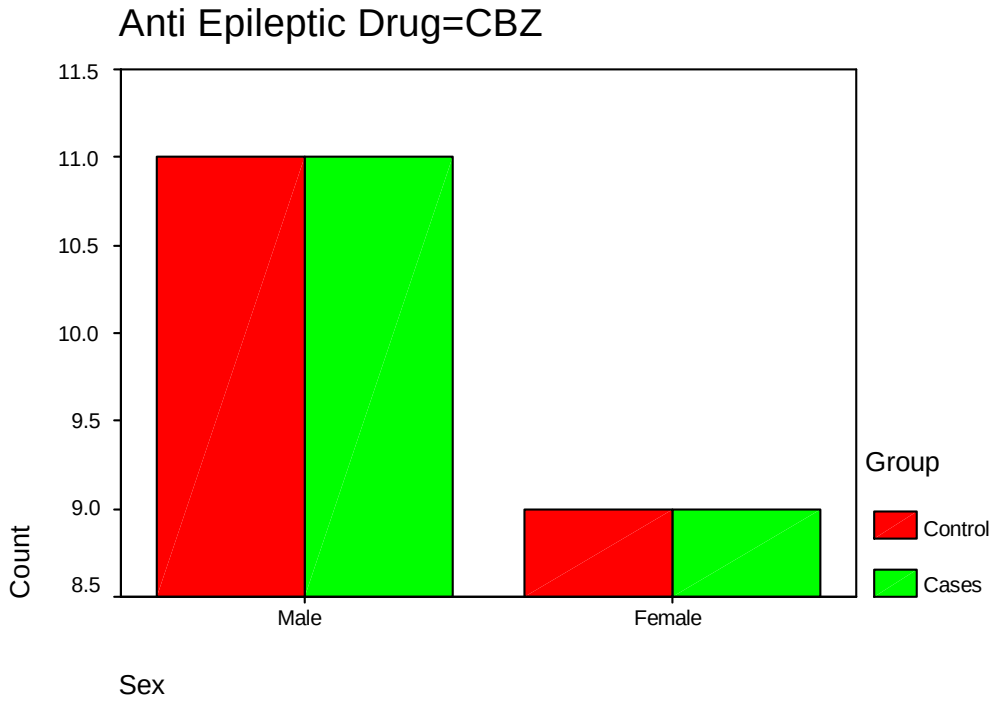
In the carbamazepine group, which includes the cases and controls, there were 25 children in the age group of 2-4 yrs, 13 children in the age group 4-6yrs, and 2 in the age group above 6yrs.



Sex * Group * Anti Epileptic Drug

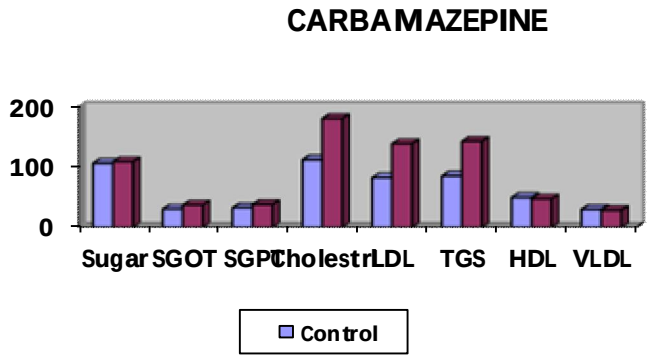
There were 22 boys and 18 girls in the carbamazepine group including both cases and controls, making a total of 40.

SEX	GROUP		TOTAL	P Value
	CASES	CONTROL		
MALE	11	11	22	1.000
FEMALE	9	9	18	
TOTAL	20	20	40	



Comparison of variables in the Anti Epileptic drug – carbamazepine group

	Group				P Value
	Control		Cases		
	Mean	SD	Mean	SD	
Sugar	106.55	19.41	109.00	25.15	0.732
SGOT	30.45	7.64	37.15	12.99	0.054
SGPT	32.75	10.22	38.05	9.51	0.098
Cholestrl	112.15	13.55	180.50	28.06	0.000
LDL	82.45	12.12	138.85	22.55	0.000
TGS	85.40	6.29	142.80	9.48	0.000
HDL	49.65	6.34	47.25	6.06	0.228
VLDL	29.90	5.96	28.30	8.24	0.486



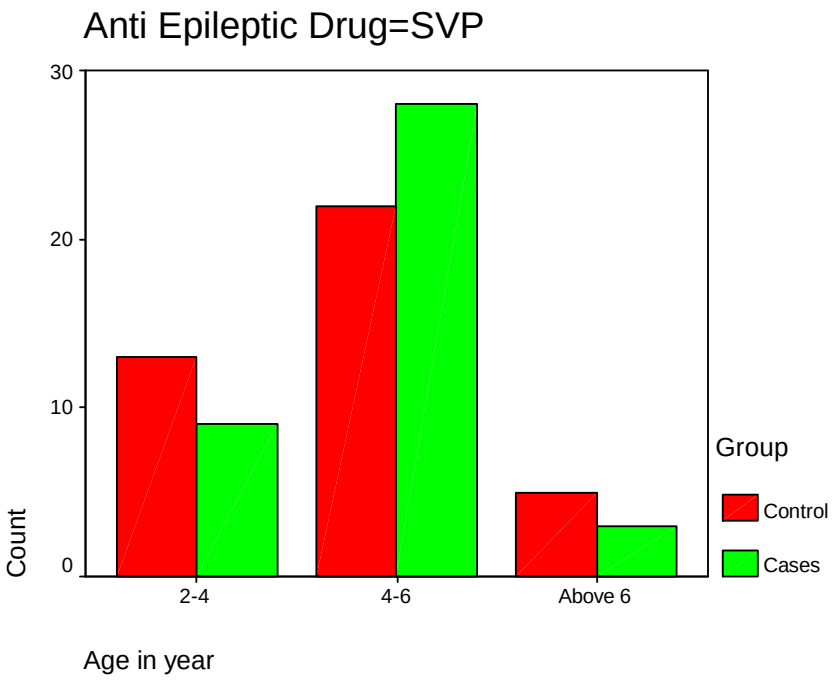
In the carbamazepine group, sugar, SGOT and SGPT levels did not alter with in the cases and control groups, whereas the total cholesterol, LDL-C, triglycerides levels were significantly elevated with the p value of 0.000 (highly significant) when compared with the controls. There were no significant alterations seen in the level of HDL-C and VLDL-C.

SODIUM VALPROATE

Age in year * Group * Anti Epileptic Drug

AGE	GROUP		TOTAL	P Value
	CASES	CONTROL		
2-4YR	13	9	22	0.378
4-6YR	22	28	50	
>6YR	5	3	8	
TOTAL	40	40	80	

There were 22 children in the age group 2-4 yrs, 50 children in the age group 4-6yrs, 8 in above 6yrs age group, coming to a total of 80 children.

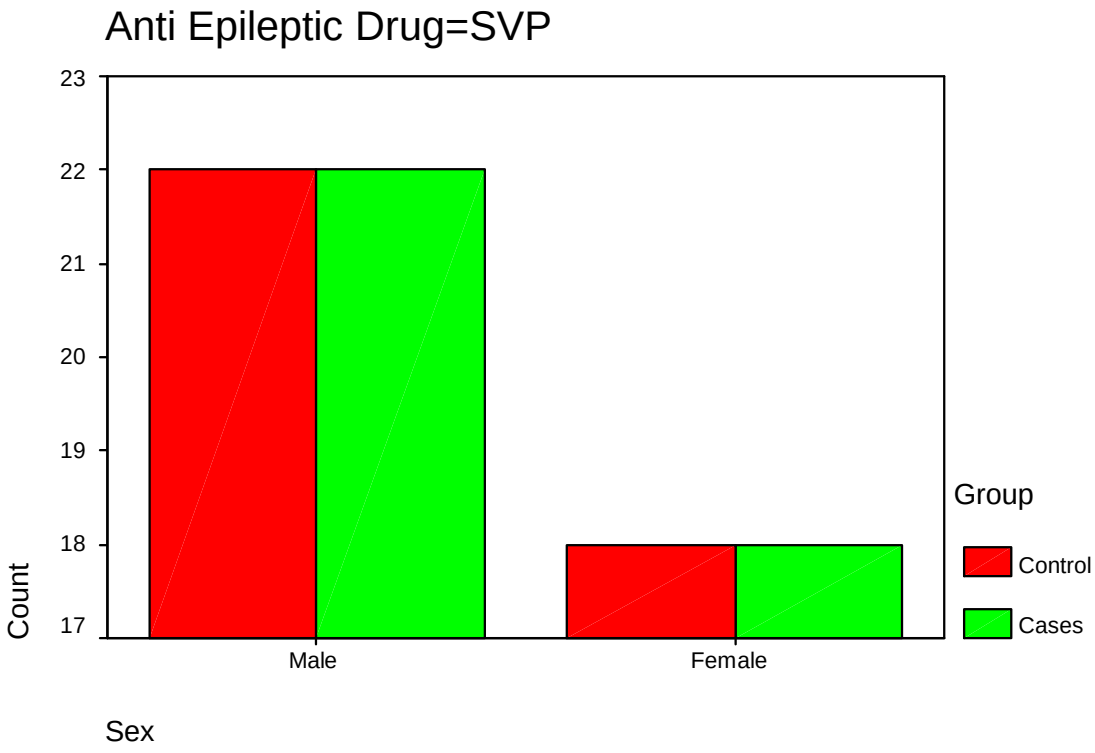


Sex * Group * Anti Epileptic Drug

SEX	GROUP		TOTAL	P Value
	CASES	CONTROL		
MALE	22	22	44	1.000
FEMALE	18	18	36	
TOTAL	40	40	80	

In the above table, 44 children who participated were boys, 35 were girls giving a total of 80 including both the cases and controls.

No statistical significance was found between the sexes in the cases and control groups.

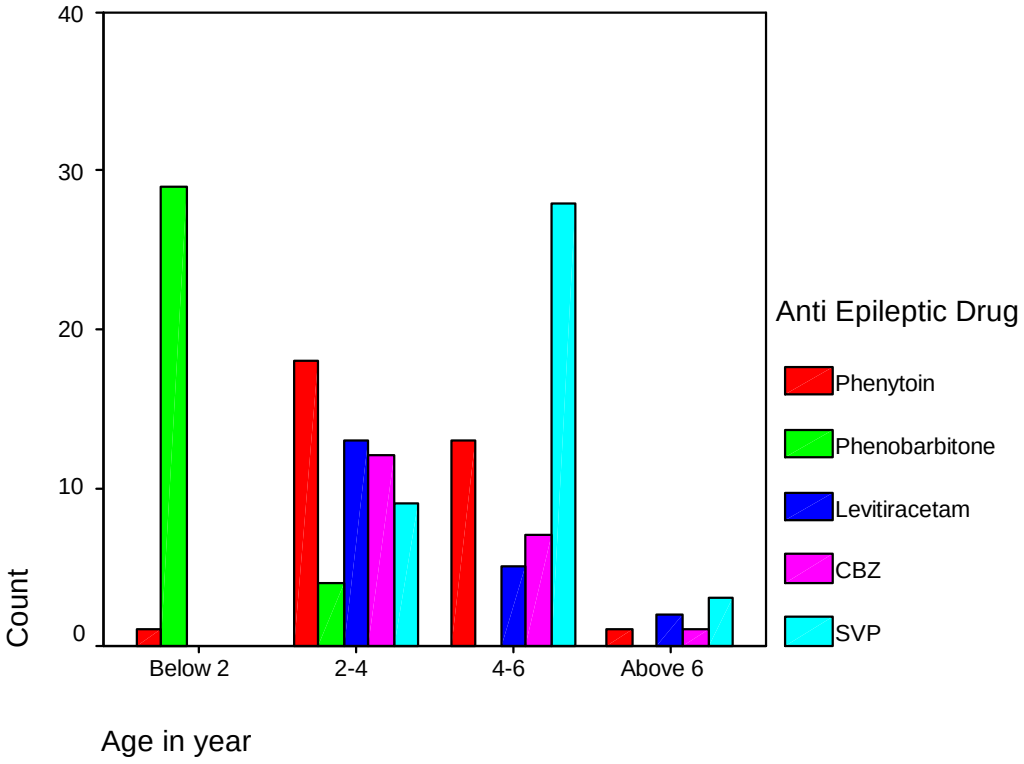


Comparison of variables in the Anti Epileptic drug – SODIUM VALPROATE group

	Group				P Value
	Control		Cases		
	Mean	SD	Mean	SD	
Sugar	110.93	28.00	113.35	19.88	0.656
SGOT	40.63	13.10	40.35	11.21	0.920
SGPT	36.50	10.61	40.70	8.81	0.058
TC	105.05	9.03	105.63	8.16	0.766
LDL	93.55	7.75	94.60	6.83	0.522
TGS	87.80	4.37	89.88	7.87	0.149
HDL	46.10	4.56	45.78	5.12	0.765
VLDL	18.26	5.97	20.85	7.16	0.083

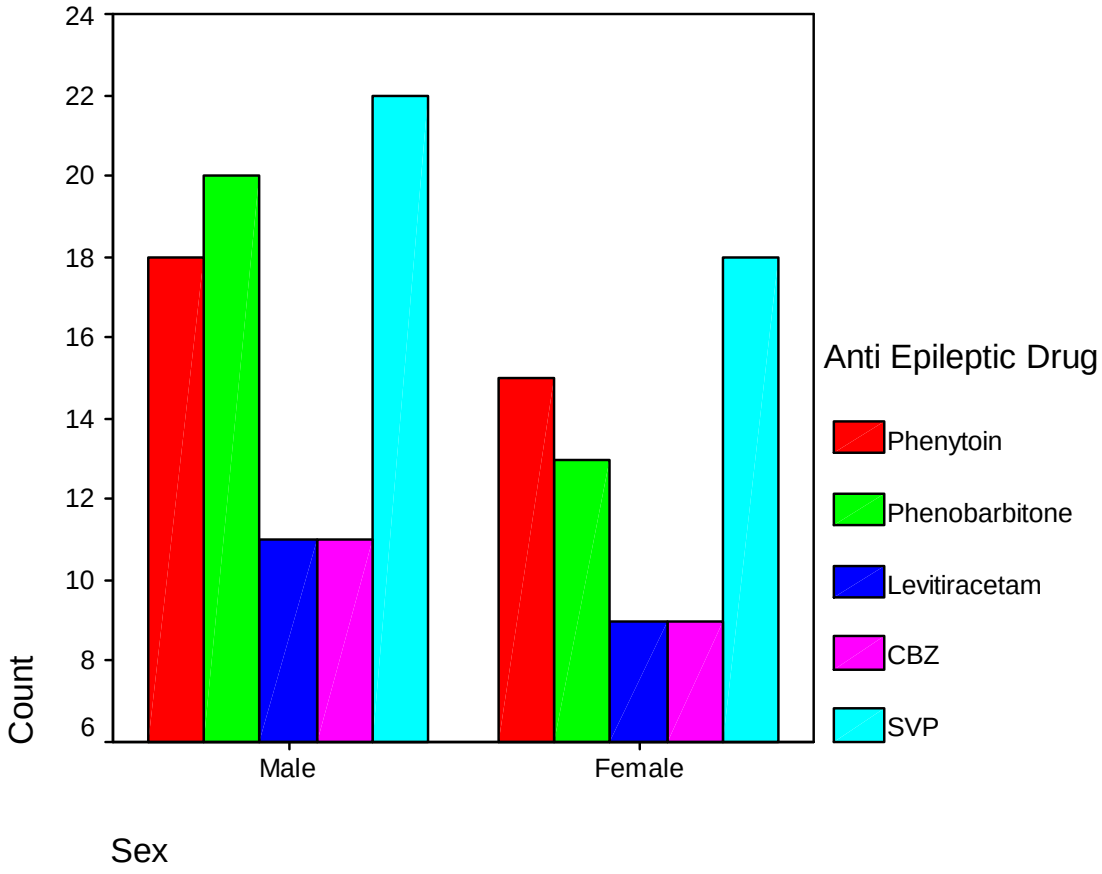
There was no statistical significance in children taking sodium valproate in the parameters like sugar, SGOT, SGPT, total cholesterol, triglycerides, LDL-C, HDL-C,VLDL-C, when compared with the control groups.

COMPARISON OF VARIOUS AGE GROUPS IN CHILDREN TAKING ANTIEPILEPTIC DRUGS



The most common age group in the phenobarbitone group was below 2yrs. In the age group between 2-4yrs the most common drug used was phenytoin. Between the age groups 4-6yrs, sodium valproate is the most commonly used drug.

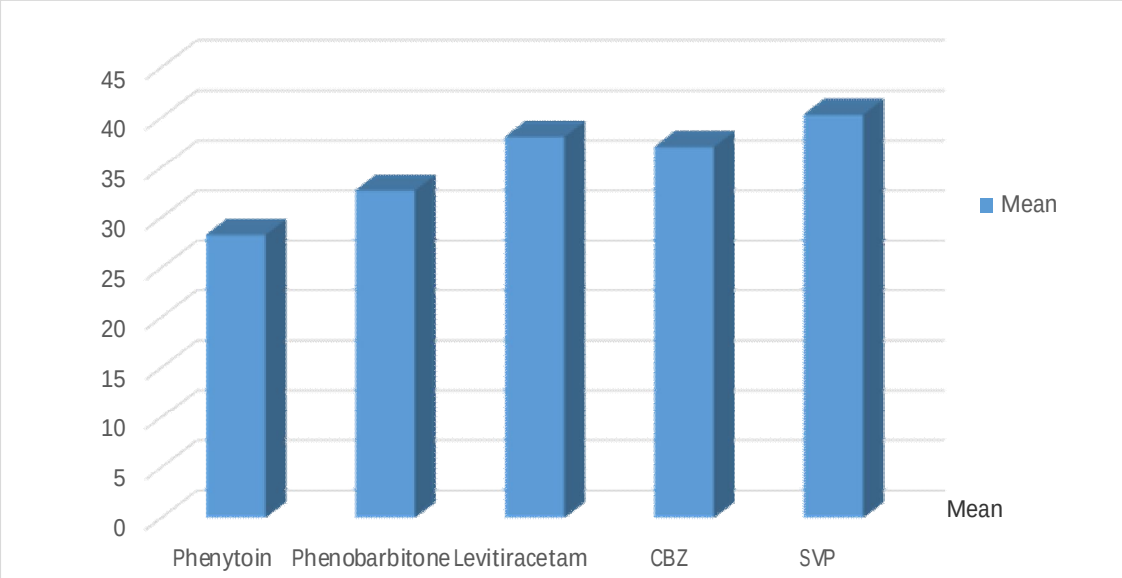
COMPARISON OF SEX IN CHILDREN TAKING ANTIEPILEPTIC DRUGS



In relation to sex, almost both male and female children were equally distributed in the various group of antiepileptic drugs compared in the study.

COMPARISON OF SIGNIFICANT RISE OF SGOT LEVELS IN CHILDREN TAKING ANTIEPILEPTIC DRUGS

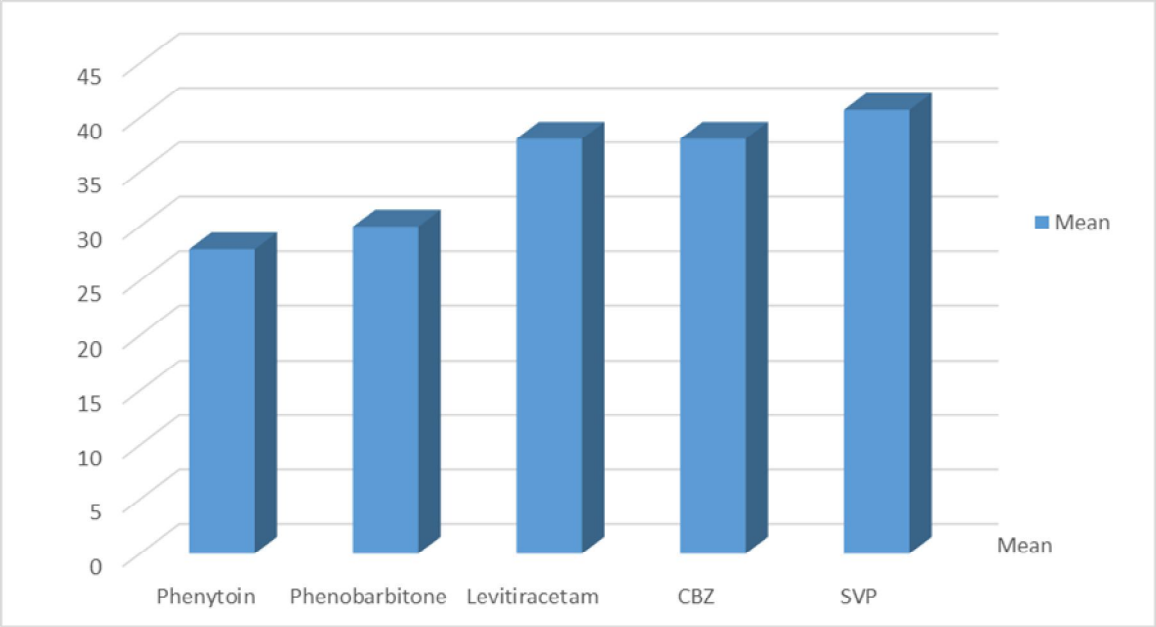
	N	Mean	Std. Deviation	Std. Error
Phenytoin	33	28.33	5.066	.882
Phenobarbitone	33	32.73	6.311	1.099
Levetiracetam	20	38.15	12.987	2.904
CBZ	20	37.15	12.987	2.904
SVP	40	40.35	11.208	1.772
Total	146	35.17	10.659	.882



On comparing the SGOT levels in various subgroups, it has been found that there has been significant alteration in the SGOT levels in the children taking sodium valproate drug.

COMPARISON OF SIGNIFICANT RISE OF SGPT LEVELS IN CHILDREN TAKING ANTIEPILEPTIC DRUGS

	N	Mean	Std. Deviation	Std. Error
Phenytoin	33	27.88	5.872	1.022
Phenobarbitone	33	29.97	5.632	.980
Levetiracetam	20	38.05	9.506	2.126
CBZ	20	38.05	9.506	2.126
SVP	40	40.70	8.809	1.393
Total	146	34.65	9.374	.776

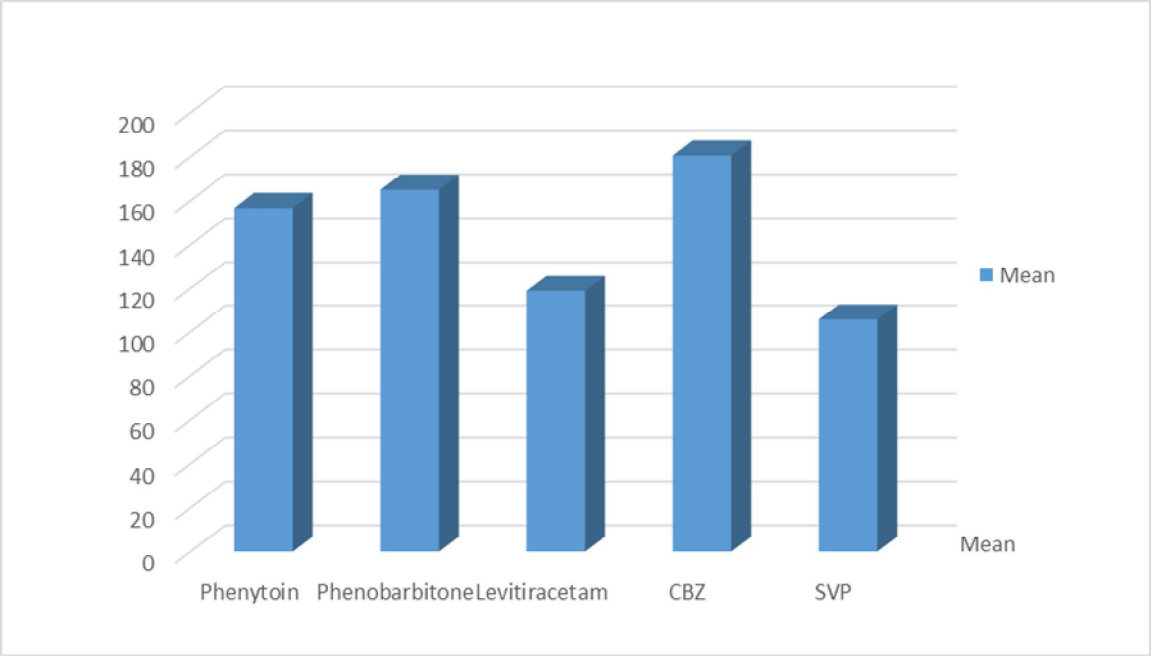


Like SGOT levels, SGPT were also significantly altered in children taking sodium valproate monotherapy when compared with that of other drug groups.

COMPARISON OF TOTAL CHOLESTEROL LEVELS IN CHILDREN TAKING ANTIEPILEPTIC DRUGS

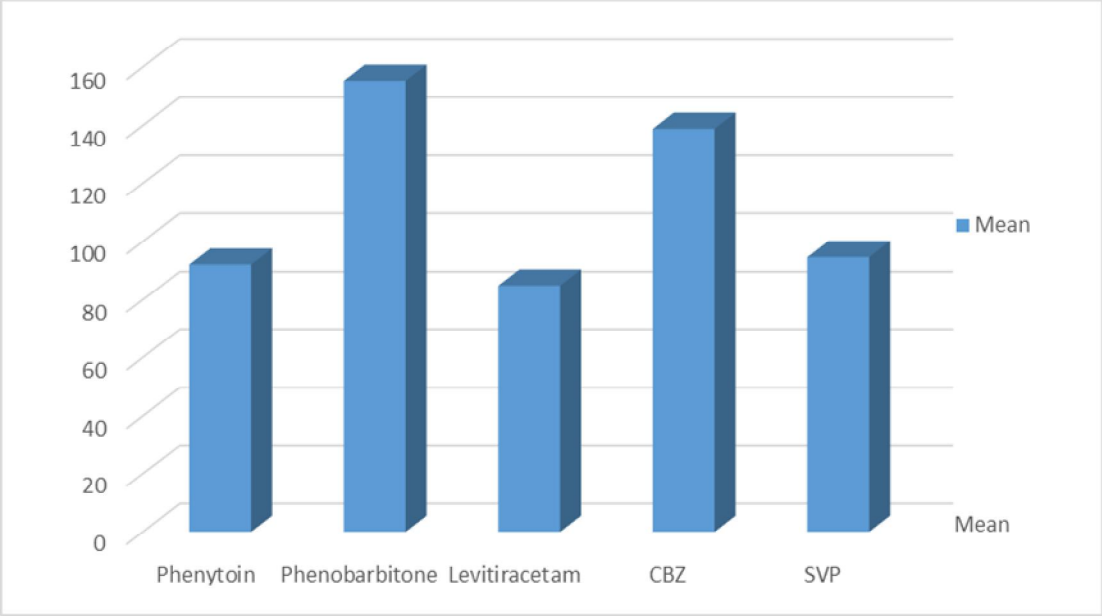
	N	Mean	Std. Deviation	Std. Error
Phenytoin	33	156.73	31.930	5.558
Phenobarbitone	33	164.97	34.414	5.991
Levetiracetam	20	118.85	10.674	2.387
CBZ	20	180.50	28.059	6.274
SVP	40	105.63	8.161	1.290
Total	146	142.66	37.878	3.135

When total cholesterol levels were compared, children taking carbamazepine group was found to have elevated levels followed by phenobarbitone group and phenytoin group.



COMPARISON OF LDL-C LEVELS IN CHILDREN TAKING ANTIEPILEPTIC DRUGS

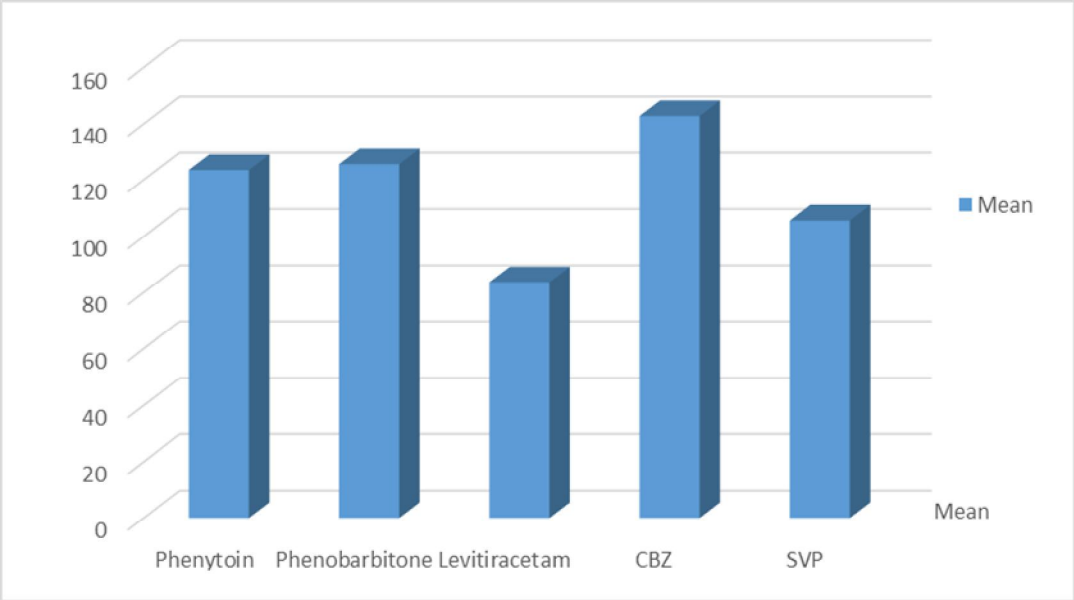
	N	Mean	Std. Deviation	Std. Error
Phenytoin	33	92.06	24.334	4.236
Phenobarbitone	33	155.27	28.547	4.969
Levetiracetam	20	84.90	11.670	2.610
CBZ	20	138.85	22.549	5.042
SVP	40	94.60	6.831	1.080
Total	146	112.47	34.760	2.877



On comparing the levels of LDL-C in the above groups, mean levels were higher in children taking phenobarbitone drug, followed by carbamazepine.

COMPARISON OF TRIGLYCERIDE LEVELS IN CHILDREN TAKING ANTIEPILEPTIC DRUGS

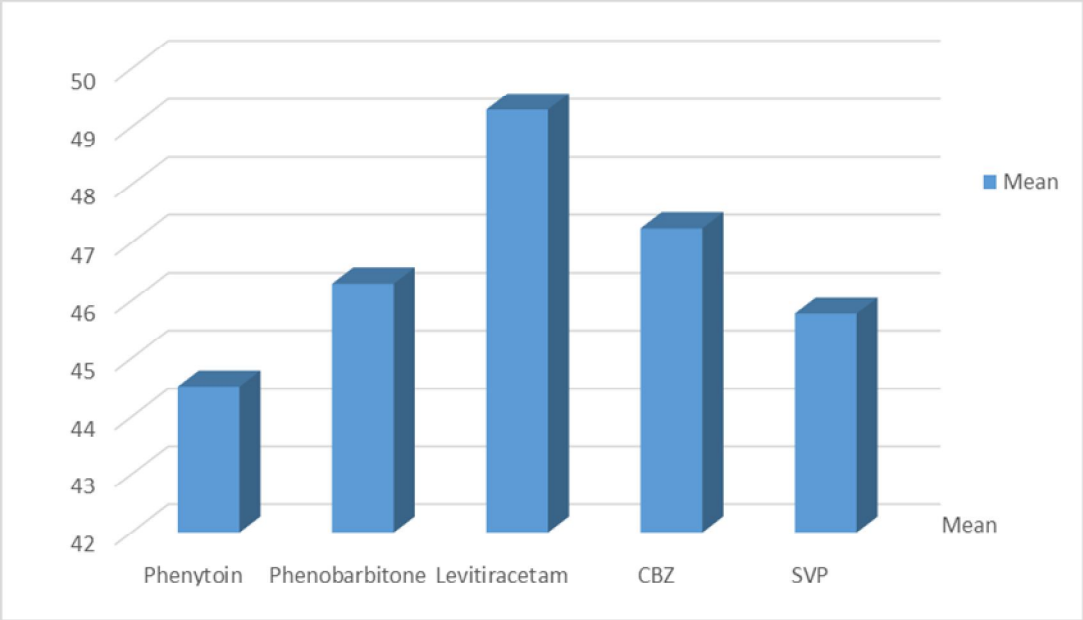
	N	Mean	Std. Deviation	Std. Error
Phenytoin	33	123.48	25.986	4.524
Phenobarbitone	33	125.55	42.194	7.345
Levetiracetam	20	83.65	6.201	1.387
CBZ	20	142.80	9.479	2.120
SVP	40	89.88	7.875	1.245
Total	146	111.93	31.999	2.648



Mean triglyceride levels were elevated in children taking carbamazepine, following by those children on phenobarbitone and phenytoin. Lowest mean levels were found in children on sodium valproate and the least levels were found with those children on levetiracetam.

COMPARISON OF HDL-C LEVELS IN CHILDREN TAKING ANTIEPILEPTIC DRUGS

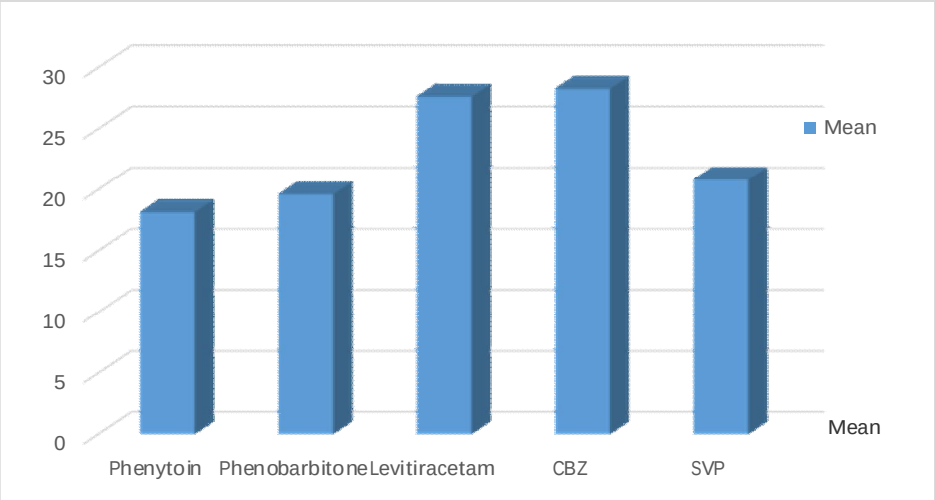
	N	Mean	Std. Deviation	Std. Error
Phenytoin	33	44.52	10.143	1.766
Phenobarbitone	33	46.30	9.465	1.648
Levetiracetam	20	49.30	5.273	1.179
CBZ	20	47.25	6.060	1.355
SVP	40	45.78	5.122	.810
Total	146	46.29	7.756	.642



Children taking Levetiracetam had the highest levels of HDL-C, when compared with other groups and the lowest levels were found in the children taking phenytoin drug.

COMPARISON OF VLDL-C LEVELS IN CHILDREN TAKING ANTIEPILEPTIC DRUGS

Drugs	N	Mean	Std. Deviation	Std. Error
Phenytoin	33	18.18	8.998	1.566
Phenobarbitone	33	19.64	8.703	1.515
Levetiracetam	20	27.65	6.612	1.478
CBZ	20	28.30	8.240	1.843
SVP	40	20.85	7.156	1.131
Total	146	21.92	8.821	.730



In the children taking carbamazepine drug, the VLDL-C levels were elevated when compared with the other children.

DISCUSSION

In this study, serum lipid profile which includes the total cholesterol, LDL-C, VLDL-C, HDL-C levels along with sugar and liver enzymes were compared in the children who were taking antiepileptic monotherapy for at least 6 months duration with that of the normal children.

Patients with epilepsy have to undergo chronic treatment with antiepileptic drugs. It is not only important that their seizures have to be under control but also adverse effects due to intake of long term antiepileptic drugs should be minimal.

Hence periodic screening of these children for any risk factors and monitoring them is essential.[12]

There were 33children in the phenytoin group, 42 for phenobarbitone group, 20 for Levetiracetam, 20 for carbamazepine and 40 for sodium valproate group. Sugar, SGOT and SGPT were not altered in both the controls and in the case group.

Statistically significant high mean TC, and TG levels were observed in the group receiving phenytoin for more than six months when compared with the control group with the mean value of 156.73 and 123.48. There was no statistical significance seen in the levels of HDL-C, LDL-C and VLDL-C.

The results were similar to the study conducted by **manimegalai et al**, where they observed statistically significant high mean TC, HDL-C, LDL-C and TG levels in the group receiving phenytoin when compared with control group.

This result was also confirmed by **Rakesh et al** who showed significantly higher level of total cholesterol in children taking phenytoin therapy. In a study done by **Kantoush et al**, children who received CBZ, PB and PHT, which are enzyme-inducing drugs, caused significant increase of serum levels of TC, LDL-C and HDL-C.

This was contrary to the study conducted by **Elena Pita Calendere**, who studied on the effect of chronic phenytoin treatment on serum lipid profile in epileptic patients and found that patients showed higher HDL cholesterol, apolipoproteins A &A1**,** GGT levels and lower LDL-C cholesterol and apolipoprotein B values.

This contradictory results were similar to the study conducted by **Aditi dhir et al,** where they concluded that the Children who took valproate had significantly higher mean serum triglyceride and total cholesterol when compared to children on phenytoin monotherapy.

In the group who received phenobarbitone, TC, TG and LDL-C were all increased in the children with the mean values of 164.97, 125.55, and 155.27 when compared with the control group. HDL-C was decreased in the case group when compared with that of the control group. VLDL-C did not alter in the phenobarbitone group.

J.M. Eiris et al, who conducted a study on effects of long-term treatment with antiepileptic-drugs on serum lipid levels in children with epilepsy. In the groups receiving carbamazepine or phenobarbitone, mean TC, LDL-C levels were higher than in the control group. But he demonstrated that in his study along with other lipid parameters HDL-C was also elevated. This is similar to the study reports by **Mohamed M kantoush et al**, Phenobarbitone causes significant increase of serum TC, LDL – C higher than controls, with no significant changes in triglycerides, VLDL-C. But in this study also HDL-C was elevated. **Yilmaz et al,**

concluded in his study that the Serum TG levels increased after 3 months of treatment with phenobarbitone and remained high after 1 year but no difference was found for TC, for HDL-C and for LDL-C values. There was no statistical significance obtained in the values of sugar, SGOT and SGPT in those children.

In our study, no statistical significance was found in the children who were on Levetiracetam. In a study conducted by **manimegalai et al**, they did not observe any statistically significant difference among mean TC, HDL-C, LDL-C and TG levels in the group receiving Levetiracetam. Only very few studies are available with the newer antiepileptic drug Levetiracetam. There is no information available about the relationship between lipid function and Levetiracetam. However, no significant effects on lipid metabolism by both Levetiracetam and sodium valporate suggest that both are non-inducer of CYP51 enzyme.

In the carbamazepine group, there was significant difference observed in TC, LDL-C and TG with the mean value of 180.50, 138.85, and 142.80. HDL-C, VLDL-C did not show any statistical difference when compared with the controls. In the study conducted by**Mohamed M kantoush et al,** CBZ caused significant increase of serum TC, LDL-C and triglycerides

compared to controls. But along with it HDL-C and VLDL-C also were raised in his study.

In the study conducted by **P KUMAR ETAL,** Patients receiving Carbamazepine had significant increase in serum levels of triglyceride and VLDL-C but no significant changes in serum levels of total cholesterol & HDL-C was observed in this group as compare to normal control.

There was no statistical difference found in sodium valproate group when sugar, SGOT, SGPT, TC, LDL-C, HDL-C, TG, VLDL-C were compared with that of the control group.

This is similar to the conclusion derived by the study conducted by **pooja dewan et al,** where there were no statistical difference were found in the cases and in the control groups with respect to the parameters like TC, LDL-C,HDL-C,TGs, VLDL-C.

MUZAMIL M MUGLOO ET AL, observed in his study that there was no statistically significant difference among mean TC, HDL-C, LDL-C,

TG, and LFT levels in the group receiving sodium valporate when compared with control group.

This is also supported by another study by **Yaser et al,** who studied on the relationship of serum lipids and thyroid hormone level changes in epileptic children on valproate mono therapy, where he concluded that Valproate has no effect on either lipids or thyroid functions in epileptic children treated with that drug.

But the results derived by **Aditi dhir et al**, were contradicting to our study where the Children who took valproate had significantly higher mean serum triglyceride and total cholesterol when compared to children on phenytoin monotherapy

CONCLUSIONS

Following conclusions were observed from the study:

1. a) **Anticonvulsant drugs especially the enzyme inducers like Carbamazepine, Phenytoin and Phenobarbitone significantly modify serum lipids in epileptic children**:

   Carbamazepine causes increase in the levels of TC, LDL-C, and TGs. Phenobarbitone increases TC, LDL-C, TGs and also lowers HDL-C. Phenytoin increases TC, TGs and lowers HDL-C.

   b) Phenytoin and Phenobarbitone lowers the HDL-C significantly. Hence children on long term therapy are at greater risk for atherogenesis.

2. **Sodium valproate and Levetiracetam did not cause significant changes in the serum lipid profile**.

3. Sodium valproate causes significant elevation of liver enzymes when compared with that of the controls**.**

LIMITATIONS OF THE STUDY:

1. Sample size is small
2. Since the time period is limited , follow up could not be done to see the trends and changes in the lipid profile.
3. Baseline lipid profile of the children was not available

RECOMMENDATIONS

1. Baseline and serial lipid profile monitoring should be done in all children who are put on Phenytoin and Phenobarbitone therapy.

2. Levetiracetam did not produce significant changes in the serum lipid profile and liver enzymes; hence it is safe to use in children for long term management of seizures.

3. Levetiracetam is the drug of choice for starting the children on long term medication if the child is suffering from deranged lipid profile, or with previous history of stroke, or has a family history of obesity, atherosclerosis, dyslipidemia, hypertension or cardiovascular disease.

4. Sodium valproate should be avoided in children who already have pre-existing liver disease, hepatic dysfunction and who are on hepatotoxic drugs.

5. Baseline LFT may be done in all children who are started on Sodium valproate and serial LFT monitoring may be done every 3-6 months.

6. Non atherogenic diet along with lifestyle modifications, at least during the time of AED therapy, should be advised during treatment with enzyme inducing drugs like Carbamazepine, Phenytoin and Phenobarbitone.

BIBLIOGRAPHY

1. K. Manimekalai1, B. Visakan, KartikJ. Salwe, S. Murugesan Evaluation of Effect of Antiepileptic Drugs on Serum Lipid Profile among Young Adults with Epilepsy in a Tertiary Care Hospital in Pondicherry.
2. BERLIT P., KRAUSE K. H., HEUCK C. C., SCHELLENBERG B. Serum lipids and anticonvulsants. *Acta Neurol.Scand*., 1982, 66 : 328-334.
3. CALANDRE E.P., RODRIGUEZ-LOPEZ C., BLAZQUEZ A., CANO D. Serum lipids, lipoproteins and apolipoproteinsA and B in epileptic patients treated with sodium valproate, carbamazepine or phenobarbitone .*Acta Neurol. Scand*., 1991, 83 : 250-253.
4. DEMIRCIOG˘LU S., SOYLU A., DIRIK E. Carbamazepine and valproic acid: effects on the serum lipids and liver functions. *Pediatric. Neurol*., 2000, 23:142-146.
5. EIRIS J. M., LOJO S., DEL RIO M. C. *et al.* Effects of long-term treatment with antiepileptic drugs on serum lipid levels in children with epilepsy. *Neurology*,1995, 45 : 1155-1157
6. FRANZONI E., GOVONI M., D'ADDATO S. *et al.* Total cholesterol, high-density lipoprotein cholesterol, and triglycerides

in children receiving antiepileptic drugs. *Epilepsia,* 1992, 33 : 932-935.

7. HELDENBERG D., HAREL S., HOLTZMAN M., LEVTOWO,TAMIR I. The effect of chronic anticonvulsant therapy on serum lipids and lipoproteins in epileptic children. *Neurology*, 1983, 33 : 510-513
8. REDDY M. N. Effect of anticonvulsant drugs on plasma total cholesterol, high-density lipoprotein cholesterol, and apolipoproteins A and B in children with epilepsy. *Proc. Soc. Exp. Biol. Med*., 1985,180 : 359-36
9. VERROTI A., DOMIZIO S., ANGELOZZI B. *et al.* Changes in serum lipids and lipoproteins in epileptic children treated with anticonvulsants. *J. Paediatr. Child. Health.*, 1997, 33 : 242-245
10. YALCIN E., HASSANZADEH A., MAWLUD K. The effects of long-term anticonvulsive treatment on serum lipid profile. *Acta Paediatr. Jpn*., 1997, 39 : 342-345.
11. ZEITLHOFER J., DOPELBAUER A., TRIBL G., LEITHA T.,DECKE L. Changes of serum lipid patterns during long-term anticonvulsive treatment. *Clin.Investig*., 1993, 71 : 574-578.

12. Aditi Dhir, Suvasini Sharma1, Puneet Jain, Bhanu K. Bhakhri Satinder Aneja parameters of metabolic syndrome in Indian children with epilepsy on valproate or phenytoin monotherapy
13. POOJA DEWAN, ANJU AGGARWAL AND FARIDI; Effect of Phenytoin and Valproic Acid Therapy on Serum Lipid Levels and Liver Function Tests
14. E. YILMAZ, Y. DOS¸ AN, M. K. GÜRGÖZE and S. GÜNGÖR;Serum lipid changes during anticonvulsive treatment
15. Nadkarni J1, Uikey D, Sharma U, Dwivedi R; Effect of Antiepileptic drugs on lipid profile in children with Epilepsy.
16. AYNACI F. M., ORHAN F., OREM A., YILDIRIMIS¸Effect of antiepileptic drugs on plasma lipoprotein (a) and other lipid levels in childhood. *J. Child. Neurol*., 16 : 367-36
17. Journal of Clinical and Diagnostic Research. 2014 Aug, Vol-8(8): HC05-HC09 Rakesh Kumar, Prasant Sharma1, Rajiv Ranjan1, Rajlaxmi Mundhra
18. study of clinical profile and biochemical parameters in children on antiepileptic drugs: a brain-liver-kidney tri-axis in epilepsy, Open Journal of Medicine & Healthcare (OJMH),Vol. 1, No. 3, December 2016, pp. 11~22.ISSN: 2456-2866
19. Aditi Dhir, Suvasini Sharma, Puneet Jain, Bhanu K. Bhakhr, Satinder Aneja,Parameters of metabolic syndrome in Indian

children with epilepsy on valproate or phenytoin monotherapy/ Jul-Sep / Volume 10 / Journal of Pediatric Neurosciences / 223

20. Mohamed M. Kantoush, Azza K. El-Shahawy, Samia S. Sokker , Hanan R.Serag, Effects of Treatment with Antiepileptic Drugs on Serum Lipid Profile in Epileptic Children

21. P Kumar, M Tyagi, Y Tyagi, A Kumar, A Kumar, Y Rai. *Effect Of Anticonvulsant Drugs On Lipid Profile In Epileptic Patients*. The Internet Journal of Neurology. 2003 Volume 3 Number 1.

22. Muzamil M Mugloo, Rubeena Akhtar1, Seema Malik, Assessment of Serum Lipid Profile and Liver Function Parameters in Children with Epilepsy on Phenytoin or Valproic Acid Monotherapy for 6 Months and Beyond

23. Fatma Mujgan Sonmez, Ercan Demir, Asim Orem, Sermet Yildirmis, Fazil Orhan, Adnan Aslan and Murat Topbas, Topbas,Effect of Antiepileptic Drugs on Plasma Lipids, Lipoprotein (a), and Liver Enzymes, *J Child Neurol* 2006 21: 70

24. J.M. Eiris, MD; S. Lojo, PhD; M.C. Del Rio, PhD; I. NOVOM, D;M. Bravo, MD; P. Pavon, MD; and M. Castro-Gago, MD,Effects of long-term treatment with antiepileptic-drugs on serum lipid levels in children with epilepsy, NEUROLOGY 1995;45:1155-1157

25. Geoffrey F. Gibbons The Role of Cytochrome P450 in the Regulation of Cholesterol Biosynthesis

26. Hasan Tekgul1, Nilgun Demir and Sarenur Gokben Serum Lipid Profile in Children Receiving Anti-epileptic Drug Monotherapy: Is it Atherogenic? Journal of Pediatric Endocrinology & Metabolism, 19, 1151-1155 (2006)

27. Nelson's Textbook of Pediatrics, Nineteenth Edition, 2: 2823

DATA COLLECTION FORM

Study Id –

OP no. -

Name -

Age -

Sex - **1**: Male **2**: Female **3**: Others

HISTORY

Duration of epilepsy a) in years and months-

Drug history: Name:

Duration:

Dosage:

Family history of seizures:

Family history of stroke/atherosclerosis:

ANTHROPOMETRY

Height a)

Weight a)

BMI:

INVESTIGATIONS

1. Glucose:
2. Liver Enzymes:
3. Serum triglyceride a) value- b) Category – Normal/borderline/Elevated
4. Total cholesterol – a) value – b) Category – Normal /borderline/Elevated
5. LDL cholesterol – a) value - b) Category – Normal /borderline/Elevated
6. HDL cholesterol – a) value – b) Category – Normal /Decreased
7. VLDL cholesterol – a) value - b) Category - Normal /borderline/Elevated

PATIENT INFORMATION SHEET

Place of study: - DEPARTMENT OF GENERAL PEDIATRICS AND DEPARTMENT OF PEDIATRIC NEUROLOGY, ICH.

Name of Investigator: Dr. PON DIVYA

Name of Participant: **Age**: **Sex**:

Hospital No:

Study title:

"**EFFECT OF ANTIEPILEPTIC DRUGS ON SERUM LIPID PROFILE AMONG CHILDREN WITH EPILEPSY IN A TERTIARY CARE HOSPITAL"**

We request your child to participate in the study.

Aim of the study-

To study the relationship between serum lipid levels and antiepileptic drugs

Methods-

On arrival your child will be subjected to a basic clinical proforma following which 3ml of venous blood will be drawn and sent to biochemistry lab for estimation of serum lipid levels.

Can I refuse to participate in the study?

Participation in the study is purely voluntary. You may refuse to participate or withdraw from the study at any time. In both cases the treatment and care your child receives from this hospital will not be affected in any manner.

Benefits and harms of participating in the study-

Your child will not benefit directly by participating in this study. But by way of participating in this study, your child is contributing to updation of science which may benefit her/him and all other patients with this disease in future.

Drawing 3 ml blood from your child may be perceived as harm, but medically this will not compromise her/his health. Further your child will not be poked because blood for this test will be collected along with other tests advised by your doctor.

Confidentiality-

The data collected from the study will be used for the purpose of study only. The results of the study will be published. Personal information of the children participating in the study will be kept confidential. There will not be any disclosure about your child's information without your permission.

Subject rights-

If you wish further information regarding your child's rights as a research participant, you may contact the principal investigator in the mobile number or address mentioned below.

Principal Investigator: DR PON DIVYA

Mobile number : 9710513102

Contact Address - Institute of Child Health and Hospital for Children, Halls road, Egmore, Chennai.

Place:

Date: Signature of parent

INFORMED CONSENT FORM

Study place: DEPARTMENT OF GENERAL PEDIATRICS AND DEPARTMENT OF PEDIATRIC NEUROLOGY, ICH.

Title of the study: "EFFECT OF ANTIEPILEPTIC DRUGS ON SERUM LIPID PROFILE AMONG CHILDREN WITH EPILEPSY IN A TERTIARY CARE HOSPITAL"

Name of the investigator: DR PON DIVYA

Name of the Participant: **Age**: **Sex**:

Hospital number:

1. I have read and understood the patient information sheet provided to me regarding the participation of my child in the study.

2. I have been explained about the nature of the study and had my questions answered to my satisfaction.

3. I have been explained about my rights and responsibilities by the investigator.

4. I will allow my child to cooperate with the investigator and undergo clinical tests subjected during the study whole heartedly.

5. I have been advised about the risks associated with my child's participation in this study.*

6. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my child's future treatment in this hospital. *

7. I hereby give permission to the investigators to release the information obtained from my child as result of participation in this study to medical journals/conference proceedings.

8. I understand that my child's identity will be kept confidential if my child's data are publicly presented/published.

9. I have decided my child can participate in the research study. I am aware that if I have any question during this study, I should contact the investigator.

10. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

Name and signature / thumb impression of the parent/guardian

Name _____ Signature_____

Date_____

Name and Signature of the investigator

Name _____ Signature_____

Date_____

Name and Signature of impartial witness 1:

Name _____ Signature_____

Date_____

Name and Signature of impartial witness 2:

Name _____ Signature_____

Date_____

study id	name	age in mont	sex	type o	name of aed	duration in mont	dose-mg/kg/d	family h/o seizure	family h/o stroke or CAD	HEIGHT	WEIGHT	sugar	sgot	sgpt	cholestrl	ldl	tgs	hdl	vldl
1		36	m		PHENYTOIN	6	4	no	no	102	14	95	25	30	178	97	125	50	11
2		38	f		PHENYTOIN	8	5	no	no	105	12	96	27	25	175	95	142	45	23
3		40	m		PHENYTOIN	7	5.5	no	no	106	11	89	28	28	124	93	102	46	15
4		48	m		PHENYTOIN	12	7	yes	no	110	13	86	24	27	176	114	110	50	7
5		36	m		PHENYTOIN	17	6	no	no	105	12	75	30	24	160	92	132	53	17
6		48	m		PHENYTOIN	11	7.5	no	no	104	13	74	31	31	182	93	110	34	26
7		60	m		PHENYTOIN	6.5	6	no	no	105	12	87	28	19	150	87	107	42	21
8		72	m		PHENYTOIN	7.5	5	no	no	100	11	86	29	18	145	79	99	32	12
9		48	m		PHENYTOIN	8.5	5.5	yes	no	102	15	92	35	25	158	89	181	53	22
10		48	m		PHENYTOIN	9.5	6.25	no	yes	104	16	112	32	28	182	100	136	50	9
11		62	m		PHENYTOIN	10	6	no	no	108	15.2	102	35	29	152	102	134	36	18
12		74	f		PHENYTOIN	6	7	no	no	110	14.5	152	30	35	154	123	107	69	11
13		60	f		PHENYTOIN	7	5.25	no	no	119	13	140	34	31	136	75	142	36	22
14		72	f		PHENYTOIN	8.5	5	no	no	120	13.5	132	19	40	162	74	126	42	14
15		48	f		PHENYTOIN	9	4.75	no	no	114	13	102	20	32	186	85	110	45	11
16		24	f		PHENYTOIN	10	5.75	no	no	110	13	110	24	31	176	86	120	34	22
17		36	f		PHENYTOIN	7	6.25	no	no	102	12.5	136	21	30	187	98	135	39	14
18		42	f		PHENYTOIN	12	7.3	yes	no	105	13	150	22	29	167	98	98	51	18
19		41	f		PHENYTOIN	17	8.5	no	no	103	14	124	26	25	120	72	103	46	11
20		49	f		PHENYTOIN	12	7	yes	no	105	14	140	28	29	143	69	104	39	13
21		54	f		PHENYTOIN	8	6.5	no	no	102	15	98	24	24	149	86	134	43	12
22		60	m		PHENYTOIN	6	6.75	no	yes	102	16	96	35	21	132	91	106	42	10
23		50	m		PHENYTOIN	5.6	6.25	no	no	105	15	95	30	28	97	72	112	53	20
24		41	f		PHENYTOIN	7	5.85	no	no	100	14.5	97	35	29	128	61	134	52	27
25		44	f		PHENYTOIN	9	5.25	no	no	112	14	78	40	30	175	124	102	34	17
26		40	m		PHENYTOIN	16	5.75	yes	no	102	13	79	36	36	130	82	106	39	12
27		42	f		PHENYTOIN	24	6.85	yes	no	100	12.5	75	32	30	153	76	103	57	40
28		41	m		PHENYTOIN	13	7.75	no	no	115	15	74	28	34	145	91	142	59	33
29		40	f		PHENYTOIN	6	6.65	no	no	120	14.5	76	24	40	127	91	106	60	14
30		52	m		PHENYTOIN	8	6.5	no	no	110	14	65	27	15	285	202	223	38	45
31		52	m		PHENYTOIN	9	6	no	no	102	13.5	68	26	19	161	76	110	32	12
32		53	m		PHENYTOIN	10	4.65	yes	no	110	14	98	25	20	152	89	120	50	10
33		54	m		PHENYTOIN	11	5.65	no	no	111	13	120	25	28	125	76	154	18	31

controls:				HEIGHT	WEIGHT	sugar	sgot	sgpt	cholestrl	ldl	tgs	hdl	vldl
1		36	m	102	14	121	25	36	100	80	75	40	10
2		38	f	105	12	132	32	32	117	82	74	41	12
3		40	m	106	11	104	26	32	120	84	86	42	14
4		48	m	110	13	115	28	35	105	85	85	41	16
5		36	m	105	12	140	37	24	108	86	84	40	15
6		48	m	104	13	121	34	27	110	90	85	45	17
7		60	m	105	12	82	28	28	95	92	95	46	14
8		72	m	100	11	87	27	34	96	95	98	50	18
9		48	m	102	15	69	22	31	89	94	92	52	19
10		48	m	104	16	78	35	30	110	91	91	51	14
11		62	m	108	15.2	74	36	19	112	96	93	58	15
12		74	f	110	14.5	72	44	25	114	98	95	65	17
13		60	m	119	13	65	40	24	115	97	98	65	20
14		72	f	120	13.5	80	38	29	117	99	99	65	25
15		48	f	114	13	115	37	30	110	97	97	64	28
16		24	f	110	13	114	12	32	108	95	78	62	24
17		36	m	102	12.5	132	16	40	109	85	79	63	27
18		45	f	105	13	102	22	35	100	86	96	68	30
19		41	f	103	14	142	20	30	98	84	95	70	32
20		44	f	105	14	122	27	40	95	85	79	72	35
21		54	f	102	15	120	29	26	96	96	64	74	25
22		60	m	102	16	131	30	27	93	95	62	78	13
23		50	m	105	15	115	34	39	86	100	56	75	30
24		51	f	100	14.5	95	25	38	100	95	80	56	35
25		44	f	112	14	97	22	34	104	88	101	60	25
26		52	m	102	13	96	30	39	117	95	100	65	27
27		42	f	100	12.5	93	39	36	100	100	98	64	28
28		41	m	115	14	91	34	27	108	101	99	65	24
29		40	f	120	13	90	33	29	109	104	99	66	25
30		63	m	110	12.5	88	30	31	105	100	79	54	15
31		52	m	102	15	64	19	37	110	101	89	45	12
32		74	m	110	14.5	97	22	34	110	102	94	42	16
33		54	m	111	16	113	28	32	100	103	105	28	10

study id	name	age in month	sex	type of e	name of aed	duration in months	dose-mg/k	family h/o seizure	family h/o stroke or	HEIGHT	WEIGHT	sugar	sgot	sgpt	cholestrl	ldl	tgs	hdl	vldl
1		8	m		phenob	6	4	no	no	78	7	95	35	34	178	136	74	60	11
2		10	f		phenob	8	5	no	no	79	8	96	20	32	175	135	100	45	23
3		9	m		phenob	7	5.5	no	no	80	8	89	25	26	165	122	78	42	15
4		24	m		phenob	12	5	yes	no	82	8	86	31	30	150	130	85	50	20
5		27	f		phenob	17	5	no	no	70	9.5	75	35	31	170	112	132	55	17
6		17	f		phenob	11	4.5	no	no	80	8	74	32	32	180	125	114	34	26
7		9	m		phenob	6.5	4	no	no	72	7	87	35	36	198	140	107	44	31
8		9.5	m		phenob	7.5	5	no	no	70	8	86	40	28	158	141	65	32	12
9		11.5	f		phenob	8.6	5.5	yes	no	75	9	92	41	26	152	138	181	53	22
10		11.5	f		phenob	9.4	3	no	yes	78	9.5	112	20	22	170	136	134	56	19
11		17	m		phenob	10	3.5	no	no	65	9	102	28	26	140	127	134	36	18
12		9	m		phenob	6	3.75	no	no	68	7.5	152	31	24	150	134	110	69	11
13		10	f		phenob	7	5.25	no	no	75	8	140	35	30	120	120	140	38	22
14		11	m		phenob	8.5	5	no	no	78	7	132	20	26	198	122	126	42	16
15		14	m		phenob	9	4.75	no	no	80	9	102	25	28	154	125	110	45	11
16		17	f		phenob	10	5.75	no	no	75	8	110	40	32	144	123	198	36	22
17		11	f		phenob	7	4.5	no	no	74	9	136	33	40	144	185	174	39	17
18		24	m		phenob	12	4.3	yes	no	83	10	150	36	38	165	196	96	51	18
19		25	m		phenob	17	5.5	no	no	78	12	124	38	35	155	178	103	48	11
20		24	m		phenob	12	4	yes	no	85	10	140	36	40	182	186	104	39	13
21		17	m		phenob	8	4.5	no	no	75	9	98	35	34	200	178	154	43	18
22		15	m		phenob	6	4	no	yes	76	7	96	32	40	250	182	106	46	10
23		10	f		phenob	6.5	3.5	no	no	70	6.5	95	38	28	180	190	99	53	20
24		11	f		phenob	7	3.75	no	no	75	6.5	97	36	26	128	195	259	52	30
25		17	f		phenob	9	4.25	no	no	70	9	78	34	34	175	185	114	34	17
26		24	f		phenob	16	4.75	yes	no	74	11	79	36	32	130	178	106	39	12
27		29	m		phenob	24	2.9	yes	no	90	12	75	38	34	153	165	125	60	40
28		29	m		phenob	13	3.75	no	no	86	10	74	28	32	120	170	142	62	32
29		10	m		phenob	6	4.5	no	no	75	7.5	76	26	20	127	166	106	45	14
30		11	m		phenob	8	5	no	no	74	6.5	65	42	21	285	202	223	39	40
31		15	f		phenob	9	5.5	no	no	76	9	68	43	22	161	178	110	32	12
32		15	m		phenob	10	4.65	yes	no	80	8	98	26	28	152	189	90	54	10
33		21	m		phenob	11	5.65	no	no	78	9	120	30	22	135	135	144	55	38

controls:				HEIGHT	WEIGHT	sugar	sgot	sgpt	cholestrl	ldl	tgs	hdl	vldl
1		17	m	77	8	110	35	34	100	80	82	40	10
2		15	f	80	7.5	94	37	28	117	82	84	41	12
3		11	m	82	8.5	97	38	35	120	84	86	42	14
4		24	m	80	9	95	35	33	105	85	85	41	16
5		20	f	74	10	85	36	32	108	86	84	40	15
6		15	f	80	9	87	30	30	110	90	85	45	17
7		9.5	m	70	7.5	65	25	29	120	92	95	46	14
8		11.5	m	75	8.5	115	24	27	130	95	98	50	18
9		12.6	m	77	8.5	120	30	19	120	94	92	52	19
10		10.5	f	74	8	114	32	32	110	91	91	51	14
11		15.5	m	68	8	123	20	20	112	96	93	58	15
12		11	m	64	7.5	130	21	28	114	98	95	98	17
13		17	f	73	8	132	24	15	115	97	98	65	20
14		13	m	75	7	140	25	25	117	99	99	65	25
15		16	m	78	9	112	26	29	110	97	97	64	28
16		19.5	m	73	8	110	22	35	108	95	78	62	24
17		14	f	72	8.5	112	21	30	109	85	79	63	27
18		22	m	80	9	127	20	26	100	86	96	68	30
19		27	m	77	12.5	124	27	28	98	84	95	70	32
20		21	m	83	11	98	28	29	95	85	85	72	35
21		18.5	m	72	10	97	30	35	96	96	82	74	25
22		15.5	m	74	8	96	32	34	93	95	80	78	13
23		22	f	68	6.5	82	30	36	86	100	75	75	30
24		7	f	72	7.2	74	32	39	100	95	72	56	35
25		18.5	m	74	8.6	77	33	41	104	88	78	60	25
26		22	f	76	12	79	36	32	117	95	79	65	27
27		27.5	m	88	10	98	35	35	100	100	85	64	28
28		26.5	m	82	11	92	25	36	108	101	86	65	24
29		12.5	m	74	8.5	90	27	25	109	104	90	66	25
30		13.6	m	72	7	85	28	29	105	100	70	54	15
31		15.4	f	78	8.5	86	29	24	110	101	75	45	12
32		19.4	m	85	7.5	115	31	26	110	102	94	42	16
33		22.4	m	80	8	125	19	27	100	103	85	28	10

study id	name	age in months	sex	type of epileps	name of aed	duration in mon	dose-mg/kg/d	family h/o seizure	family h/o stroke or CA	HEIGHT	WEIGHT	sugar	sgot	sgpt	cholestrl	ldl	tgs	hdl	vldl
1		48	m		levi	24	20	no	no	97	17	95	45	54	120	85	90	45	20
2		36	f		levi	8	15	no	no	110	22	96	20	42	110	95	95	40	22
3		60	m		levi	35	25	no	no	98	15	89	25	26	115	100	96	42	25
4		65	f		levi	38	30	yes	no	100	15	86	35	36	120	96	80	41	28
5		36	m		levi	84	35	no	no	105	18	75	60	50	132	93	85	46	26
6		38	f		levi	6	40	no	no	120	19	74	62	52	120	98	84	45	32
7		35	m		levi	6.5	15	no	no	122	18	87	35	36	112	97	89	48	30
8		45	f		levi	7.5	20	no	no	112	20	86	45	44	102	94	75	50	34
9		70	m		levi	35	25	yes	no	100	19	92	54	50	142	95	76	52	38
10		41	m		levi	9.5	22	no	yes	132	30	112	50	52	120	85	80	50	39
11		40	m		levi	10	15	no	no	130	35	102	28	26	120	86	82	56	35
12		84	f		levi	41	18	no	no	95	15	152	61	50	123	75	88	56	27
13		65	f		levi	25	25	no	no	120	20	140	35	30	140	74	85	57	20
14		75	m		levi	35	26	no	no	125	22	132	20	26	132	56	83	58	25
15		70	m		levi	26	35	no	no	105	17	102	25	28	120	68	82	50	26
16		41	f		levi	7	30	no	no	122	20	110	40	42	125	84	83	52	30
17		29	m		levi	6.8	40	no	no	105	18	136	43	40	112	82	90	45	32
18		36	f		levi	9.2	45	yes	no	100	19	150	36	38	132	86	75	52	22
19		38	f		levi	12	25	no	no	112	20	124	38	35	140	75	78	51	12
20		41	m		levi	9	28	yes	no	100	18	140	46	44	120	74	77	50	30

controls:				HEIGHT	WEIGHT	sugar	sgot	sgpt	cholestrl	ldl	tgs	hdl	vldl
1		48	f	97	17	110	35	49	122	75	85	46	20
2		36	f	110	22	96	27	51	110	90	95	40	22
3		52	f	98	15	94	35	54	115	100	95	42	25
4		54	f	100	15	98	36	21	130	96	80	41	28
5		36	m	105	18	85	40	25	132	93	90	46	26
6		50	m	120	19	75	24	27	120	90	95	44	32
7		35	m	122	18	69	19	26	105	95	96	48	30
8		45	f	112	20	112	25	31	102	94	80	48	32
9		65	m	100	19	110	27	35	142	95	85	52	36
10		41	f	132	30	115	35	38	115	80	84	50	30
11		40	m	130	35	128	50	40	120	86	89	60	33
12		76	m	95	15	135	49	21	123	70	75	56	27
13		65	f	120	20	149	40	19	96	74	76	57	28
14		72	m	125	22	95	35	26	102	52	80	58	27
15		70	m	105	17	94	37	28	104	68	82	65	24
16		41	m	122	20	98	32	34	100	75	88	65	30
17		31	m	105	18	86	22	35	110	82	85	45	32
18		36	m	100	19	84	24	32	110	85	83	68	22
19		36	f	112	20	77	29	30	95	75	82	65	29
20		40	f	100	18	78	27	29	90	74	83	70	36

study id	name	age in month	sex	type of e	name of aed	duration in mon	dose-mg/kg/d	family h/o seizure	family h/o stroke or CAD	HEIGHT	WEIGHT	sugar	sgot	sgpt	cholestrl	ldl	tgs	hdl	vldl
1		49	m		cbz	24	4	no	no	90	12	95	45	54	180	136	142	45	22
2		38	f		cbz	8	6	no	no	80	8.5	96	20	42	165	135	152	40	21
3		58	m		cbz	35	5	no	no	93	14	89	25	26	182	122	132	42	24
4		62	f		cbz	34	8	yes	no	92	12	86	35	36	175	130	132	41	25
5		38	m		cbz	7	7	no	no	80	7	75	60	50	220	112	150	46	23
6		41	f		cbz	6	4.5	no	no	78	7	74	62	52	250	125	142	45	23
7		34	m		cbz	6.5	5.6	no	no	82	7	87	35	36	165	140	152	48	30
8		45	f		cbz	7.5	6.5	no	no	80	8	86	45	44	230	141	143	50	34
9		70	m		cbz	34	7.5	yes	no	84	12	92	54	50	185	138	145	52	38
10		41	m		cbz	9.5	8.5	no	yes	82	9	112	50	52	202	136	148	50	39
11		35	m		cbz	10	9	no	no	80	8	102	28	26	165	127	155	56	35
12		79	f		cbz	41	7.5	no	no	95	12	152	61	50	135	134	140	56	45
13		62	f		cbz	25	8.2	no	no	92	11.5	140	35	30	190	120	160	57	20
14		63	m		cbz	34	5.6	no	no	95	14	132	20	26	155	122	154	58	25
15		60	m		cbz	26	35	no	no	90	12	102	25	28	156	125	142	50	26
16		40	f		cbz	7	6.5	no	no	82	7	110	40	42	162	123	135	44	32
17		28	m		cbz	6.8	7.5	no	no	80	7.5	136	43	40	152	185	138	42	40
18		34	f		cbz	9	5.25	yes	no	82	9	150	36	38	167	196	122	41	22
19		30	f		cbz	13	8	no	no	83	9.5	124	38	35	182	178	140	40	12
20		32	m		cbz	9.5	6.75	yes	no	84	6.5	140	46	44	192	152	132	42	30

controls:				HEIGHT	WEIGHT	sugar	sgot	sgpt	cholestrl	ldl	tgs	hdl
1		47	f	97	17	85	41	39	122	75	85	46
2		38	f	110	22	84	27	52	110	90	95	40
3		54	m	98	15	83	30	45	115	100	95	42
4		62	m	100	15	95	38	42	130	96	80	41
5		36	m	105	18	96	35	41	132	93	90	46
6		41	f	120	19	79	34	20	120	90	95	44
7		34	m	122	18	68	36	25	105	95	96	48
8		45	m	112	20	112	20	24	102	94	80	48
9		68	m	100	19	110	19	32	142	95	85	52
10		41	f	132	30	132	17	30	115	80	84	50
11		32	f	130	35	120	22	54	120	86	89	60
12		79	f	95	15	125	25	40	123	70	75	56
13		60	f	120	20	130	28	19	96	74	76	57
14		63	m	125	22	134	24	25	102	52	80	58
15		60	m	105	17	127	40	22	104	68	82	55
16		37	m	122	20	115	41	26	100	75	88	56
17		28	f	105	18	118	38	27	110	82	85	45
18		32	m	100	19	105	35	30	110	85	83	58
19		30	m	112	20	107	32	32	95	75	82	45
20		30	f	100	18	106	27	30	90	74	83	46

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study id	name	age in months	sex	type of ep	name of aed	duration in mon	dose-mg/kg/d	family h/o seizure	family h/o stroke or C	HEIGHT	WEIGHT	sugar	sgot	sgpt	cholestrl	ldl	tgs	hdl	vldl
1		46	m		svp	6	10	no	no	100	16	102	45	54	100	80	81	45	10
2		52	f		svp	8	12	no	no	117	17	123	20	42	105	82	82	46	12
3		61	m		svp	7	15	no	no	120	15	131	25	26	110	84	86	42	14
4		64	m		svp	12	16	yes	no	105	14	140	35	36	105	85	85	41	16
5		72	f		svp	18	14	no	no	108	20	105	60	50	108	86	84	55	15
6		48	f		svp	11	20	no	no	110	16	98	62	52	105	90	85	50	17
7		61	m		svp	6.5	25	no	no	100	18	88	35	36	95	92	88	46	14
8		70	m		svp	7.5	28	no	no	117	15	114	45	44	96	95	89	52	18
9		53	f		svp	8.4	30	yes	no	120	14	110	54	50	89	94	90	52	19
10		36	f		svp	9.6	15	no	yes	105	16	99	50	52	103	91	85	51	14
11		84	m		svp	10	14	no	no	108	15	120	28	26	102	96	84	50	15
12		60	m		svp	6.5	20	no	no	110	18	132	61	50	104	98	86	45	17
13		66	f		svp	7.5	25	no	no	100	16	142	35	30	110	97	87	42	20
14		65	m		svp	8.5	28	no	no	117	20	117	20	26	117	99	88	55	25
15		47	m		svp	9	27	no	no	120	15	103	25	28	110	97	84	40	28
16		53	f		svp	10	30	no	no	105	16	115	40	42	108	95	78	45	24
17		62	f		svp	7	29	no	no	108	17	126	43	40	109	85	79	45	27
18		67	m		svp	12	35	yes	no	110	15	98	36	38	100	86	96	42	30
19		72	m		svp	17	20	no	no	100	14	96	38	35	98	84	95	45	32
20		48	m		svp	13	24	yes	no	117	20	95	46	44	95	85	80	46	35
21		60	m		svp	8	15	no	no	120	16	92	45	44	96	96	90	48	25
22		72	m		svp	6.5	10	no	yes	105	18	88	42	40	93	95	80	49	13
23		53	f		svp	7.5	12	no	no	108	15	74	40	42	86	100	88	42	30
24		36	f		svp	8.5	16	no	no	110	14	80	40	50	100	95	78	40	35
25		85	f		svp	9	18	no	no	100	16	102	50	52	104	88	75	42	25
26		62	f		svp	16	20	yes	no	117	15	108	52	54	117	95	80	44	27
27		66	m		svp	23	22	yes	no	120	18	119	40	44	100	100	90	45	28
28		65	f		svp	11	25	no	no	105	16	121	41	42	108	101	85	45	24
29		47	f		svp	6	40	no	no	108	20	136	40	40	109	104	84	43	25
30		52	m		svp	8.5	25	no	no	110	15	140	42	43	105	100	79	44	15
31		61	m		svp	9.4	35	no	no	100	16	97	43	42	110	101	89	45	12
32		67	m		svp	10.3	30	yes	no	117	17	89	26	28	110	102	85	42	16
33		70	f		svp	11.4	15	no	no	120	15	112	50	52	100	103	88	28	10
34		47	m		svp	6.5	20	no	no	105	14	152	61	50	117	95	80	55	27
35		58	m		svp	7.5	25	no	no	108	20	140	35	30	100	100	88	50	28
36		59	f		svp	8.6	29	no	no	110	16	132	20	26	108	101	87	51	24
37		52	f		svp	9.4	30	no	no	100	18	102	25	28	109	104	90	52	25
38		35	m		svp	11	25	no	no	117	15	110	40	42	105	100	79	44	15
39		85	m		svp	7.5	30	no	no	120	14	136	43	40	110	101	89	45	12
40		59	f		svp	13	35	yes	no	105	16	150	36	38	110	102	94	42	16

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controls:				HEIGHT	weight	sugar	sgot	sgpt	cholestrl	ldl	tgs	hdl
1		40	f	100	16	99	36	41	110	78	85	40
2		62	f	117	17	102	35	45	120	82	90	41
3		51	f	120	15	114	24	46	105	84	91	50
4		48	m	105	14	158	56	51	106	78	80	41
5		64	m	108	20	157	52	24	114	86	90	40
6		52	m	110	16	162	42	35	110	90	92	45
7		48	f	100	18	132	63	34	95	79	90	46
8		63	m	117	15	123	61	36	96	95	80	45
9		58	f	120	14	128	70	45	89	94	85	44
10		37	m	105	16	129	25	42	110	85	84	46
11		72	m	108	15	140	28	40	112	96	89	48
12		54	m	110	18	96	32	12	114	98	75	48
13		44	f	100	16	82	37	32	114	97	76	45
14		46	f	117	20	84	41	20	117	90	80	40
15		37	m	120	15	75	46	25	110	92	82	41
16		50	m	105	16	69	67	26	110	95	88	48
17		80	f	108	17	94	54	28	109	85	85	42
18		72	f	110	15	55	51	32	100	86	83	45
19		75	m	100	14	112	40	35	98	84	82	47
20		85	m	117	20	132	30	40	99	85	83	48
21		58	f	120	16	120	21	42	96	96	90	56
22		63	m	105	18	125	28	28	93	95	86	48
23		59	f	108	15	128	26	24	88	100	88	59
24		37	f	110	14	120	24	35	100	95	80	45
25		75	m	100	16	126	26	31	104	88	82	46
26		64	m	117	15	135	28	50	117	95	88	47
27		72	m	120	18	145	27	48	100	100	85	50
28		85	f	105	16	152	32	46	108	101	83	55
29		49	m	108	20	143	30	62	109	104	82	46
30		54	m	110	15	122	31	58	85	100	83	48
31		60	m	100	16	101	42	50	110	101	80	39
32		57	f	117	17	98	40	37	110	102	82	42
33		51	f	120	15	75	52	32	85	103	88	45
34		44	m	105	14	84	51	34	117	95	85	50
35		38	m	108	20	97	47	45	100	100	83	45
36		48	f	110	16	99	49	40	108	101	82	42
37		42	f	100	18	85	51	31	109	104	83	50
38		36	m	117	15	69	53	23	105	100	88	54
39		72	f	120	14	65	46	28	110	101	89	45
40		65	m	105	16	105	31	27	110	102	90	42